

THE
CIRCULATORY DISTURBANCES
OF THE
EXTREMITIES

*INCLUDING GANGRENE, VASOMOTOR AND
TROPHIC DISORDERS*

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NEW YORK CITY

*WITH 192 ILLUSTRATIONS
FIVE IN COLORS*

PHILADELPHIA AND LONDON
W. B. SAUNDERS COMPANY

1924

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TO

DR. WILLIAM J. MAYO
whose masterly surgery has stimulated

and to

DR. EMANUEL LIBMAN
whose unusual medical insight has inculcated
a spirit of research

THIS VOLUME IS RESPECTFULLY INSCRIBED

PREFACE

PERHAPS in no other department of medicine has clinical diagnosis offered greater difficulties to the practitioner than in the domain of circulatory, vasomotor, and trophic disturbances of the extremities. When the author began his pathological studies of the vessels of the extremities in gangrene from whatever cause some eighteen years ago, he was not a little surprised to note what confused notions regarding clinical classification existed in the minds of some of the best internists, neurologists, and surgeons. Chronic rubor associated with obstructive arterial disease was reported as evidencing an identity of pathogenesis in such diverse clinical entities as erythromelalgia, Raynaud's disease, and thrombo-angiitis obliterans; and these three essentially different maladies were even described as of similar origin.

Whilst the recognition of thrombo-angiitis obliterans with its kaleidoscopic manifestations has had a clarifying influence, and whilst descriptions of its varied symptomatology may have contributed to a better insight into what phenomena are of neurogenic and what are of purely mechanical and hydrostatic motivation, the subject seems for many to be still enshrouded in much mystery. For, it is not only the practitioner who often fails to clearly segregate the circulatory, vasomotor, and trophic phenomena, but even in recent contributions of special investigators no dearth of misconceptions can be found.

Perhaps it is the intricacy of the physiological, anatomical, and pathological data on the one hand, and the misconstruction or misinterpretation of the perplexing objective signs on the other, that account for the lack of general comprehension.

It seemed appropriate at this juncture, therefore, to assemble, analyze, and critically interpret the maze and multitude of facts bearing on these subjects, and now at our disposal. And this with a view to establishing a correct approach and a clearer insight into both diagnosis and modes of therapy in the fields under consideration.

But the usual text-book treatment of the subject matter would, it appears to the author, hardly suffice to give that fundamental knowledge upon which an understanding of the many varied manifestations can be built up. And so, to accomplish the purpose in view, it seemed not unwise to leave the beaten paths and to diverge and intrude with intent at considerable length into allied departments of anatomy and physiology. If, by conducting the reader through all those related, basic, and essential facts that only extensive research into many fields of the literature can disclose, the work of personal investigation be minimized and confined to the perusal of but one volume; and if, by a well chosen and well directed series of discussions the burden of comprehension be facilitated, the work herein incorporated will not have been in vain.

Although the greatest importance has been accorded the pathology and clinical manifestations of the organic vascular affections—in which domain the author's experience has been ample to elucidate many of the mooted points—it was deemed wise to give more extensive consideration to the conclusions of others in some of the fields. And so, for the exposition of the normal circulation of the extremities, of thrombosis, of the vegetative

nervous system, and of the vasomotor neuroses, the views of a number of excellent authors have been more thoroughly incorporated. To the important researches of such investigators as Beneke, Aschoff, Cassirer, Hering, Müller, Dresel, Langley and others must be given credit for much that is of fundamental importance. Since their works may be inaccessible to many American readers, their essential deductions and conclusions have occasionally been given in extenso.

It is a pleasure to give acknowledgement to Miss Caroline Kleppner and Mrs. Harry Friedman for their excellent assistance in the researches on thrombo-angiitis obliterans; and to accord credit to my secretaries, Miss Ida Lipnitz and Miss Natalie Wood for help in the preparation of the manuscript. Thanks are due to the W. B. Saunders Company for their valuable coöperation in the publication of this volume.

LEO BUERGER.

1000 PARK AVENUE, NEW YORK CITY,
May, 1924.

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THE CIRCULATORY AFFECTIONS OF THE EXTREMITIES INCLUDING GANGRENE, VASOMOTOR AND TROPHIC DISORDERS

CHAPTER I INTRODUCTION

The subject of the vascular affections and gangrene of the extremities will receive consideration together, because of the intimate and inseparable clinical bonds that link these affections together. It is by virtue of the multiplicity of causal modalities that may bring forth similar or identical phenomena, and through the overlapping of manifestations of varied origin, that intricate clinical complexes are produced. We know that gangrene may be the issue of wholly different pathologic processes resulting from the action of direct or indirect mechanical, thermal, and chemical agencies, and a variety of organic vascular disorders as well as through almost inexplicable neurogenic derangements. Many of the prodromal phenomena of diseases of wholly diverse genesis may so closely resemble each other as to produce perplexing and clinically confusing pictures. It is because of these facts, that a discussion of the ultimate and most destructive lesions of varied motivation must needs be considered in connection with, and in relation to all others that may, even though only occasionally, bring about a similar issue. Only through such a grouping and comparative study can the clinician obtain a correct appreciation, either of the origin of the phenomena themselves, or of the proper classification and recognition of the diseases in question.

We need but pause for a moment to reflect on the intricacy of that maze of factors upon which the clinical features of vascular disturbances depend, to realize that not only is a knowledge of the *modus operandi* of each and of every one of them essential, but a critical balanced judgment is necessary for purposes of clinical diagnosis. Whilst for the recognition of a valvular lesion or an area of pulmonary consolidation, relatively few fundamental anatomic, acoustic and pathologic facts are necessary, the conditions upon which the manifestations of organic vascular and vasomotor disease of the extremities depend, are exceedingly complex. Even with a thorough knowledge of the distribution of the vessels, their gross and minute morphology, their rôles as dispensers of blood, their means of substituting by-paths through existing anastomoses; and even with a thorough acquaintance with the pumping mechanism, we are not thoroughly equipped for a comprehensive, critical and analytical approach to the subject. Although the

physiologists of the past have given us an abundance of conclusions, these have been modified and amplified by recent investigators, yielding a multitude of facts. A thorough comprehension of these is a prerequisite for correct explanation of the many varied clinical manifestations.

Whilst it is relatively easy to arrive at a clear concept of the objective effects of mechanical and hydrostatic forces, the heart action, the patency of the vascular channels, and the abridgement or intensification of these forces through gravity action, there are still others of imponderable nature that are clinically known to be at work, and that have been experimentally proven capable of exerting an influence. Let us recall merely a few of these. The vasomotor mechanism with its reflex play of function, its dependency on external circumstances and even on emotional states, is capable of evoking clinical pictures of obscure nature; even more so when the two diverse factors, the mechanical or hydrostatic and the neurogenic are acting in conjunction, independently, associated or related, as the case may be. In the light of recent investigations of inherent capillary activities, a new vascular domain has loomed up as capable of participating in the clinical vascular complexes. For not only is the neuromuscular mechanism governing the arterioles and venules recognized, but to the capillaries is relegated a function of their own and one susceptible to varied impressions. Whilst the mechanical and hydrostatic factors may find a response in dilatation or constriction of capillaries when there is pressure, a plenum, or a void; and whilst a certain control (usually constrictive) of the vegetative system is not denied, local metabolic or chemical influences may bring forth a functional reply in the form of dilatation of corresponding capillary areas.

We have then in the mechanical, hydrostatic, nervous and autonomic capillary forces, a combination of partly passive, partly actively functioning links, that may intrude upon the clinical picture and make it complex and hard to interpret.

The author has, therefore, included in his treatise, not only the vascular affections that may evoke trophic and destructive tissue changes, but also those nerve or vasomotor maladies that occasionally or often call forth similar clinical symptoms.

To properly comprehend all phases of this subject, we believe that our preparatory knowledge should include a study of the following:

1. The anatomy and histology of the normal vascular apparatus of the extremities;
2. The anatomy and physiology of the nervous mechanism that controls the vessels;
3. A consideration of normal and pathological local circulation;
4. A comprehension of the origin and action of thrombosis, of mechanical and of thermal agencies on the tissues;
5. The subject of gangrene in relation to its clinical diagnostic and pathological aspects; and
6. An exposition of the clinical course of all those diseases of either organic vascular, neurovascular or vasomotor causation, that have, and still do give the physician much difficulty in clinical differentiation.

Although all of these topics will be discussed, their clinical, pathological and diagnostic phases will receive the more comprehensive consideration.

CHAPTER II

ANATOMICAL CONSIDERATIONS

In applying anatomical data to the interpretation of the circulatory affections of the extremities, the course, distribution, and anastomoses of the vessels interest us from certain special angles. What may be germane to the fundamental hypotheses and observations of the anatomist and embryologist, is of importance only in an elementary way. For a clarification of our concepts of the organic and neurogenic vascular maladies, we are more particularly concerned with the following phases of the anatomy.

1. The topographical relations of the vessels to the body surface; and
2. The normal anastomoses, and therewith the foundation for collateral blood supply.

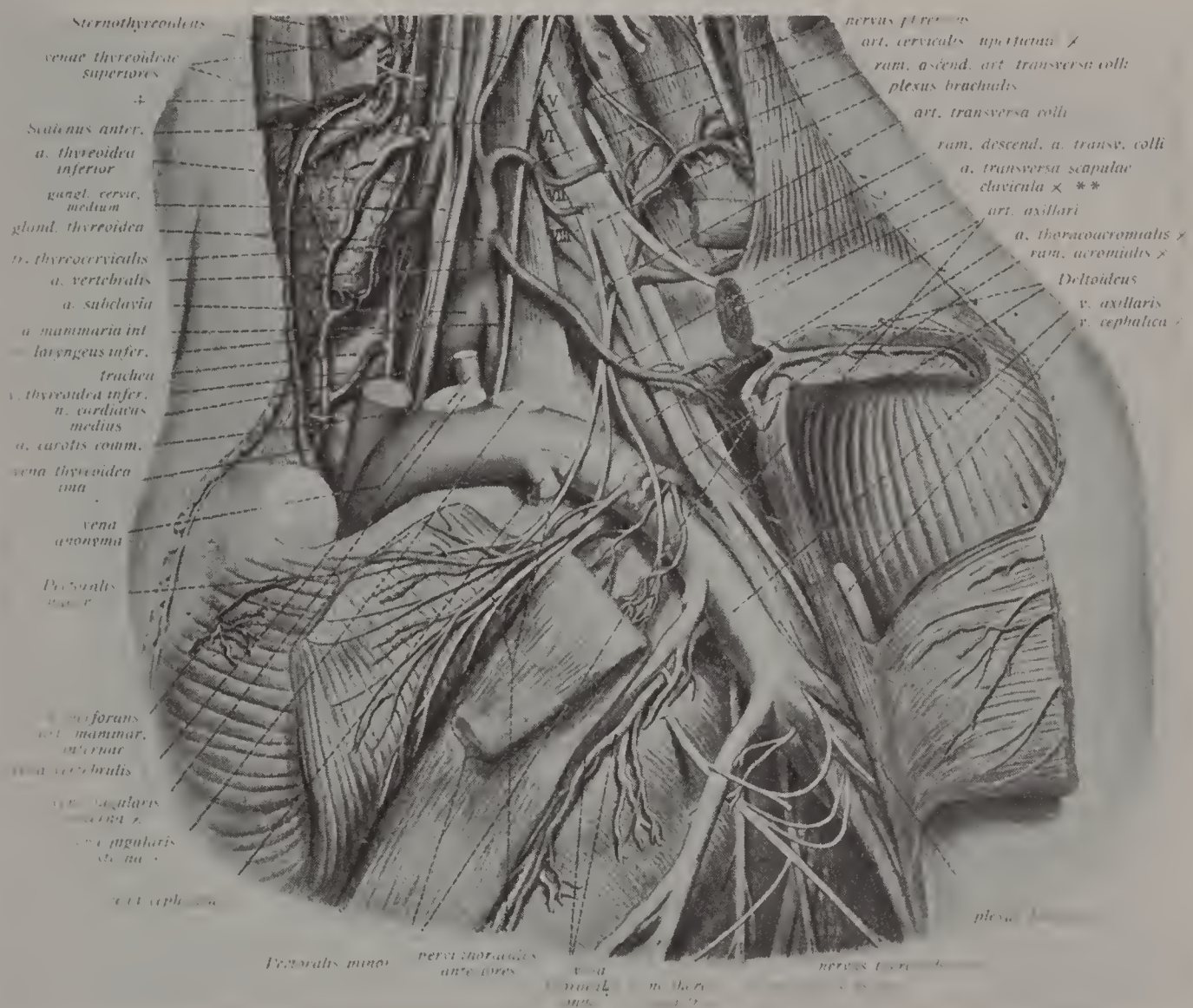


FIG. 1.—Course of the axillary artery and its branches. (Sobotta)

Diagnosis of the circulatory affections of the arteries of the extremities will be greatly facilitated through an accurate knowledge of the surface topography of the important arterial trunks supplying the peripheral parts. In order to refresh the student's memory, the essential facts necessary for the recognition of obliterated peripheral pulses will be given here. Whilst it may be easy to diagnosticate the exact points of blockage of the axillary or brachial artery by palpation alone, the patency of the larger arteries of the

lower extremities may be indeterminable by reason of their inaccessibility to the examining finger.

The Axillary Artery (*A. Axillaris*) (Fig. 1).—This is a continuation of the subclavian in its course through the axillary space. Beginning at the lower border of the first rib, in the apex of the axillary space, it courses along the outer wall of the space to the lower border of the teres major, where it is known as the brachial artery.



FIG. 2.—Course of the brachial artery. (Sobotta)

A line drawn from the middle of the clavicle to a point mid-way between the two condyles at the humerus with the arm abducted at right angles indicates its course. It may be digitally compressed in its lower or third portion (below the pectoralis minor) against the humerus just within the edge of the

coraco-brachialis and biceps. The pulsation of the axillary artery is not usually visible. In very thin individuals and in some persons after exertion especially if arteriosclerotic, the pulse may become evident with the arm lifted vertically. Palpation along the coraco-brachialis muscle in the lower part of its course just under the pectoralis minor will usually reveal the pulsation.

The *axillary vein* occupies a more superficial position and is situated toward the ulnar (posterior) side, being neither visible nor palpable under normal conditions.

The **brachial artery** (Fig. 2) is a prolongation of the axillary, beginning at the lower border of the *teres major*, and terminating just below the bend of the elbow where it divides into the radial and ulnar arteries. Above, the vessel passes along the inner side of the arm, but lower down it is deflected somewhat outward, so that in its lower part it is on the anterior surface of the brachium.

A line drawn from the junction of the outer and middle thirds of the folds of the axilla when continued to a point mid-way between the condyles of the humerus, indicates its course. In its upper two-thirds it can be felt easily and compressed against the inner side of the humerus in an outward and slightly internal direction along the internal border of the coraco-brachialis and biceps. It may pass either just along the border of this muscle or be overlapped by the inner edge of the biceps. At the middle of the arm it is also easily palpated and compressed. In the lowest third if pressure is applied backwards, it will direct it against the brachialis anticus as the latter lies over (in front of) the humerus.

For diagnostic purposes it should be remembered that the palpating finger should be directed laterally against the humerus, along the inner border of the biceps, whilst above the elbow the palpating finger must be directed backward.

With the forearm flexed at right angles and with the biceps relaxed the brachial pulse can be traced downward to within a short distance above the bend of the elbow, where compression backwards against the brachialis anticus will usually allow the plantar aspect of the fingers to detect the artery. In finding it, slight lateral displacement of the mesial border of the biceps with the tips of the palpating fingers may be necessary.

The Radial and Ulnar Arteries.—The point of bifurcation of the radial and ulnar arteries is usually so deeply situated that it is difficult to palpate the pulses in this situation, and therefore an imperceptible beat is of little clinical value.

The *ulnar artery* arises just below the bend of the elbow and passes first distally and inward beneath the muscles which arise from the internal condyle of the humerus and at the junction of the upper and middle thirds of the forearm, taking a more vertical direction. At the wrist it passes over the anterior annular ligament to the radial side of the pisiform bone and then courses across the palmar surface of the hand forming the superficial palmar arch. Three parts have been described, an antibrachial portion extending to the upper border of the anterior annular ligament; a carpal portion resting on the annular ligament; and lastly, the palmar portion.

The lowermost portion of the antibrachial course of the ulnar artery as it lies on the flexor profundus digitorum with the tendon of the flexor sublimus digitorum toward the radial side is usually the site of an ulnar pulsation.

Anomalies, however, occur that account for absence of pulsation in this region, such as those instances in which the ulnar artery is represented only by muscular branches, the vessel being substituted by a persistent median or interosseous artery. On the other hand the ulnar artery may be more superficial, passing down the forearm over, instead of under, the muscles arising from the internal condyle. Such a course may also be followed

when the artery has a normal origin, and occasionally it passes to the ulnar border of the forearm between the palmaris longus and the flexor sublimus digitorum (Cunningham).

The **radial artery** is also only palpable in its lower part between the tendon of the brachio-radialis and that of the flexor carpi radialis. Here it is very superficial, and on dissection is brought into view as soon as the fascia is divided.

The usual radial pulse may be absent when the artery passes to the dorsal surface of the arm much higher up than usual, and in such cases the super-

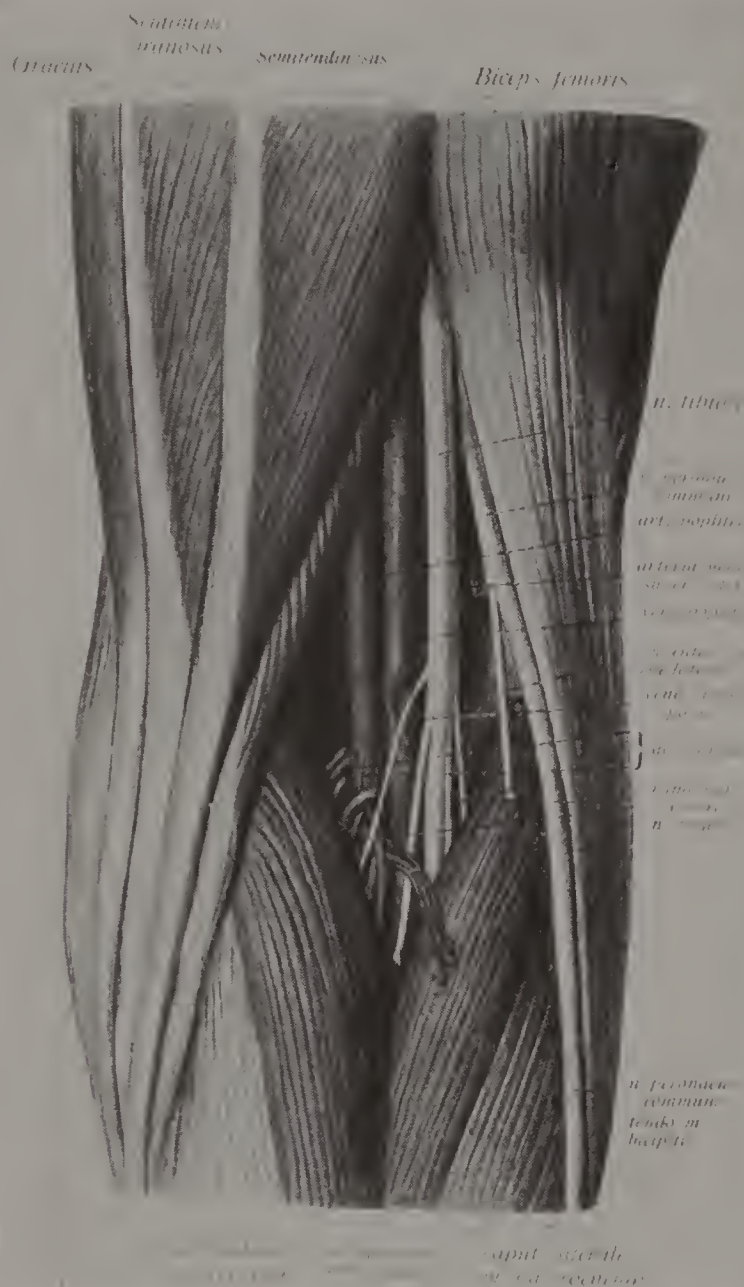
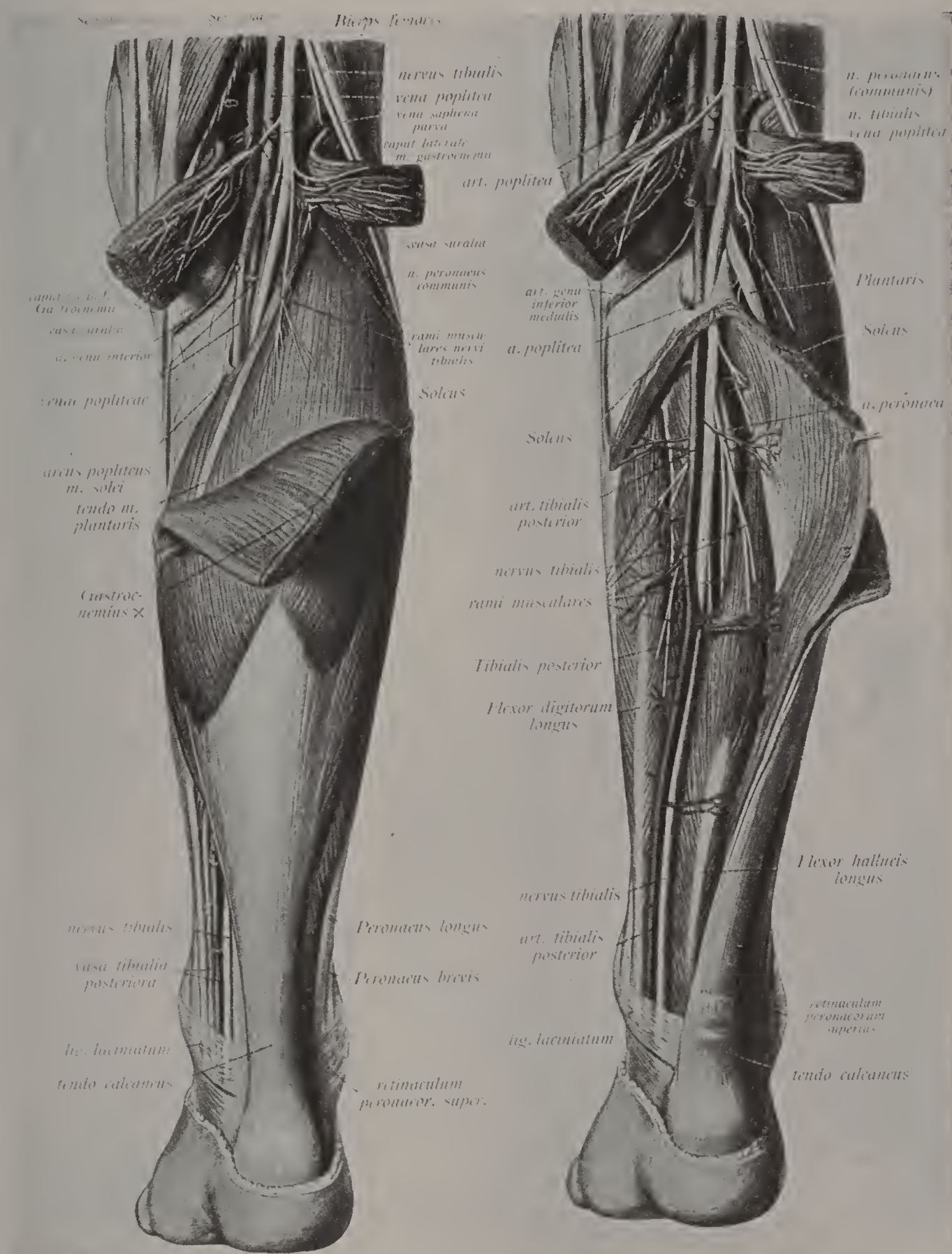


FIG. 3.—The popliteal space, with the popliteal vessels. (Sobotta)

ficial volar branch also has its origin at a higher level, and passes downward to the usual situation of the radial. In such instances it is represented by a very slender vessel, may give a very small pulse and be erroneously interpreted as indicating diminished pulsation in a radial artery.

The **femoral artery** is best felt just below the interior edge of Poupart's ligament, where the vessel can be compressed against the brim of the pelvis, just outside of the ilio-pectineal eminence. Somewhat below this it is separated from the femur by more muscle. At the apex of Scarpa's triangle it is more difficult to palpate, and the direction of pressure must be outward and somewhat backward in order to displace it against the femur. In the most accessible portion of its course just below Poupart's ligament, only slight

pressure of the finger is necessary to elicit a femoral pulse. As the pulse is traced downward, however, when a point 3 or 4 finger breadths lower is reached, more pressure is required for its detection. The normal femoral vein is neither palpable nor visible.



FIGS. 4 and 5.—Popliteal vessels and their branches at the knee posteriorly and in the leg
(*Sobotta*)

The **popliteal artery** (Fig. 3) should be palpated with the patient lying in a prone position,¹ and with the leg flexed, but relaxed at right angles. Its

¹ See p. 133.

the side to be examined is allowed to hang over the other in such a manner that the popliteal space is supported by the patella of the other leg. Then the tip of the foot of the superimposed limb may show a transmitted motion synchronous with the beat of the compressed artery.

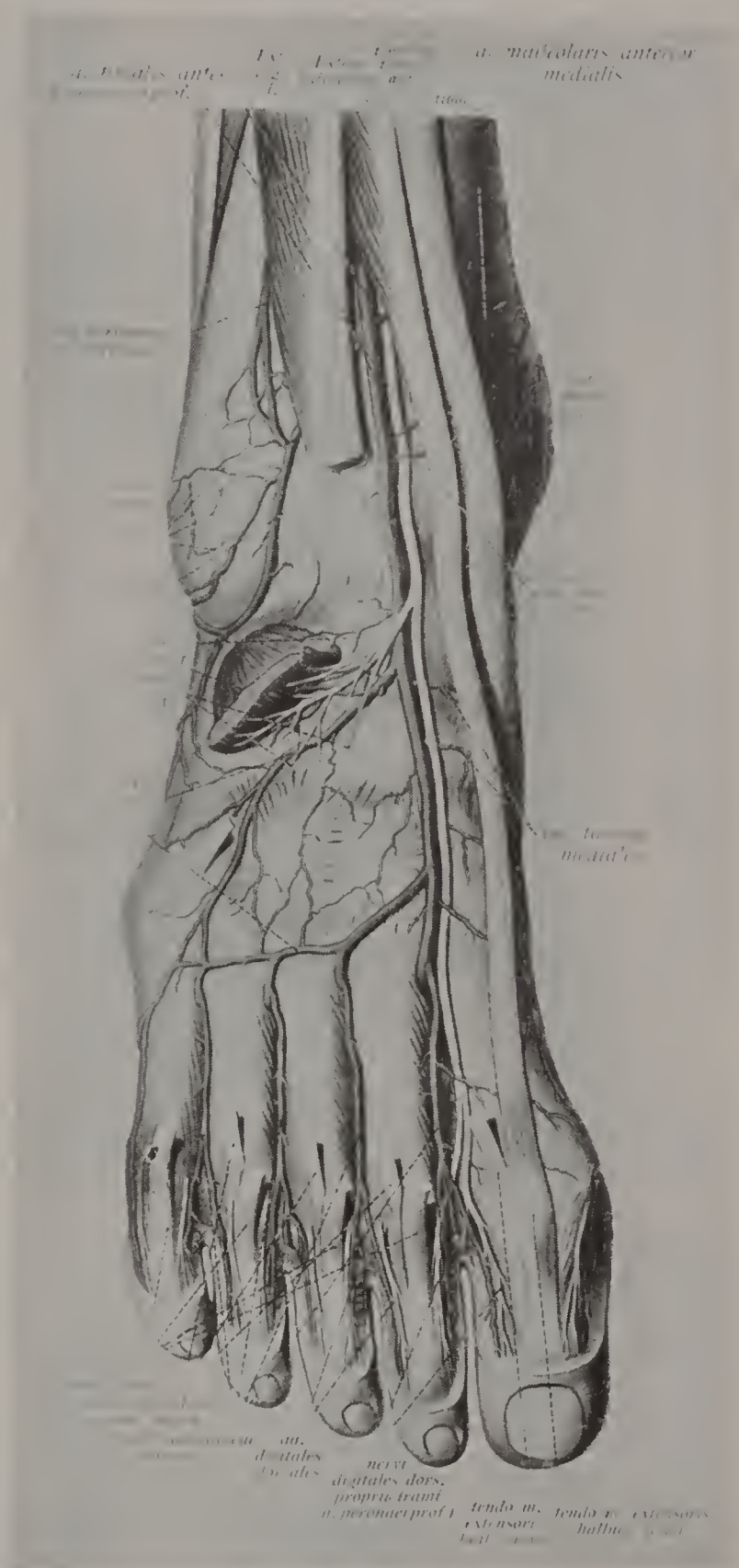


FIG. 8.—Course of the dorsalis pedis artery and its branches. (*Sobotta*)

A reference to Fig. 3 will demonstrate the relation of the popliteal artery as it takes an almost vertical direction through the popliteal space, the vein and nerve. It should be palpated just as it emerges from under the semi-membranosus muscle in the upper part of the rhomboid.

The **posterior tibial artery** (Figs. 4, 5 and 6) is a continuation of the popliteal, beginning at the bifurcation of the latter at the lower border of

the popliteus muscle and coursing downward to the groove between the internal malleolus and os calcis, where it divides into the internal and external plantar arteries.

Except for that small portion that lies immediately above the ankle, it lies very deep, being separated from the tibia by the muscles of the calf. Pulsation is perceptible only in its lower portion at the inner side of the ankle, where it lies under the deep fascia between the flexor longus digitorum and tibialis posticus tendon behind the internal malleolus. The artery can often be seen to beat between the internal malleolus of the tibia, and the mesial margin of the Achilles tendon.

The **anterior tibial artery** (Fig. 7) constitutes the other branch of the popliteal, beginning at the lower border of the popliteus muscle, passing directly forward between the tibia and fibula, over the upper border of the interosseous membrane. Then it lies in front of the latter, coursing downward to the ankle joint where it becomes the dorsalis pedis artery.

It is inaccessible to palpation except in its lowermost portion, where occasionally pulsation can be felt. Just lateral to the external border of the extensor proprius hallucis as the latter crosses the vessel obliquely, and between this and the extensor longus digitorum it becomes more superficial. Here and below this point, with the foot flexed and the extensors relaxed, some 2 inches or more of the artery frequently give a distinctly perceptible pulsation. This pulse, however, is not a constant phenomenon and for clinical purposes the beat in the dorsalis pedis is of much greater diagnostic significance.

The **dorsalis pedis artery** is a continuation of the anterior tibial artery downward to the proximal portion of the first intermetatarsal space (Fig. 8).

The artery lies just lateral to the extensor longus hallucis tendon between the latter and the mesial portion of the extensor digitorum, but closer to the former. The artery is best palpated in the region of the proximal portion of the first intermetatarsal space just lateral to the tendon of the extensor longus hallucis. If we employ the plantar aspect of the tips of 3 or 4 fingers and allow these to palpate along a line projected vertically upwards from the interspace between the great and second toes along the lateral margin of the extensor longus hallucis tendon, the normal pulsating artery will rarely escape the finger as it lies over the middle cuneiform bone. Not infrequently, particularly in moderately arteriosclerotic individuals, a visible pulse can be detected.

The Normal Anastomoses.—From a study of these, conclusions may be drawn as to the possible functional responses through existing channels, whenever one of the following modes of impediment obtain; namely, limited vascular blockage (embolic), ascending or centrally directed obturation, embolic closure with ascending and descending blockage (progressive thromboses), and localized or diffuse coarctation of the vascular lumina (atherosclerosis, endarteritis obliterans).

A more complete exposition of this subject will be found in the chapter dealing with Collateral Circulation (Chap. XII) and the diagnostic significance of the anastomoses will be dealt with in the discussions of the various arterial diseases.

CHAPTER III

THE MINUTE STRUCTURE OF THE VESSELS
THE CAPILLARIES

Simple endothelial tubes or capillaries consist of cells or elongated lanceolate plates with oval nuclei united by narrow lines of cement substance. Traced from the arteriole there is a gradual transition, the beginning of the capillaries being recognized by the final disappearance of nuclei cells. By virtue of a network of such channels distributed throughout the tissues, there is provided an excellent mode of insuring the passage of the blood in intimate contact with the tissue elements.

A nerve distribution along and surrounding them has been recognized; and while contacts between these fiber-endings and the endothelial cells have not as yet been brought to light, it is fair to assume that such junctions do indeed occur. A direct nerve supply can, therefore, be predicated for the vascular capillaries.

The endothelial layer of cells which constitutes the capillary when continued into the arteries and veins, forms the innermost layer of the intima lining these vessels. Tissue structures which differentiate the vascular areas are laid down upon this endothelium. The essential difference between the larger arteries and veins is found in the relative thickness of their walls. In the arteries smooth muscle predominates. In the veins, although a sufficiency of smooth muscle exists, there is a preponderance of white and yellow elastic tissue and the walls are not as thick.

Recent researches by Vimtrup (1922) have confirmed the existence of the contractile cells first found by Rouget (1873) in the walls of the capillaries. Mayer had described similar cells subsequently (1902), although his observations were accorded little credence.

Investigations of the activity of the capillaries of the frog's tongue (Vimtrup) led to the histologic demonstration of a meshwork of contractile cells. With suitable fixation and staining methods certain nuclei distinctly different from ordinary endothelial nuclei were discovered.

Krogh states that the form of these nuclei varies with the state of contraction of the capillary. On a dilated capillary they are broad and very thin; by contraction they become narrower and thicker, their cross-section approaching the form of a circle. The protoplasm belonging to these nuclei can be made visible by suitable staining, but even then it requires high-power immersion lenses and—especially on dilated capillaries—a good light, preferably excentric, to see it in its entirety.

On a dilated capillary the protoplasm surrounds the nucleus as a continuous layer on the capillary wall, but it diminishes in thickness towards the periphery, which is very irregular and sends out a number of very fine branches along and especially around the capillary wall. The branches show at their base a definitely triangular cross-section, but soon become flat. Sometimes they become broader and divide, but the ends are always very thin and pointed. Most of the branches lie athwart the capillary and are of such length that they reach those from the other side. Some of the branches, however, run along the capillary, and both the protoplasm and the nucleus are, as a rule, stretched in this direction.

There can be no doubt that the richly ramified muscle cells on the capillary wall are the same as those originally found by Rouget in the hyaloid membrane.

The above data warrant the conclusion (Krogh) that the capillary walls, too, consist of an endothelial tube and external muscular coat; and that the essential difference between capillaries and larger vessels is to be found in the arrangement of the muscle. In the former the musculature is repre-

sented by a wide-meshed network through which the greater part of the endothelium is free to transfer substances with a minimum of resistance; whereas in the larger arteries and veins a continuous layer of muscle is present. Even the muscular coat of the capillaries has a definite tonus subject to nervous, hormonal and other influences.

THE ARTERIOLES AND VENULES

The arterioles are situated between the arteries proper and the capillaries, and between the capillaries and the veins proper lie the venules. Some authors distinguish between an arterial and a venous capillary. Although structurally alike, one may differentiate these on a functional basis. Capillaries vary in size, but they are structurally uniform in character. The terms "arterial" and "venous" in this connection imply a change in character of the contained blood. No distinct point in the capillary net can be recognized at which such a change occurs.

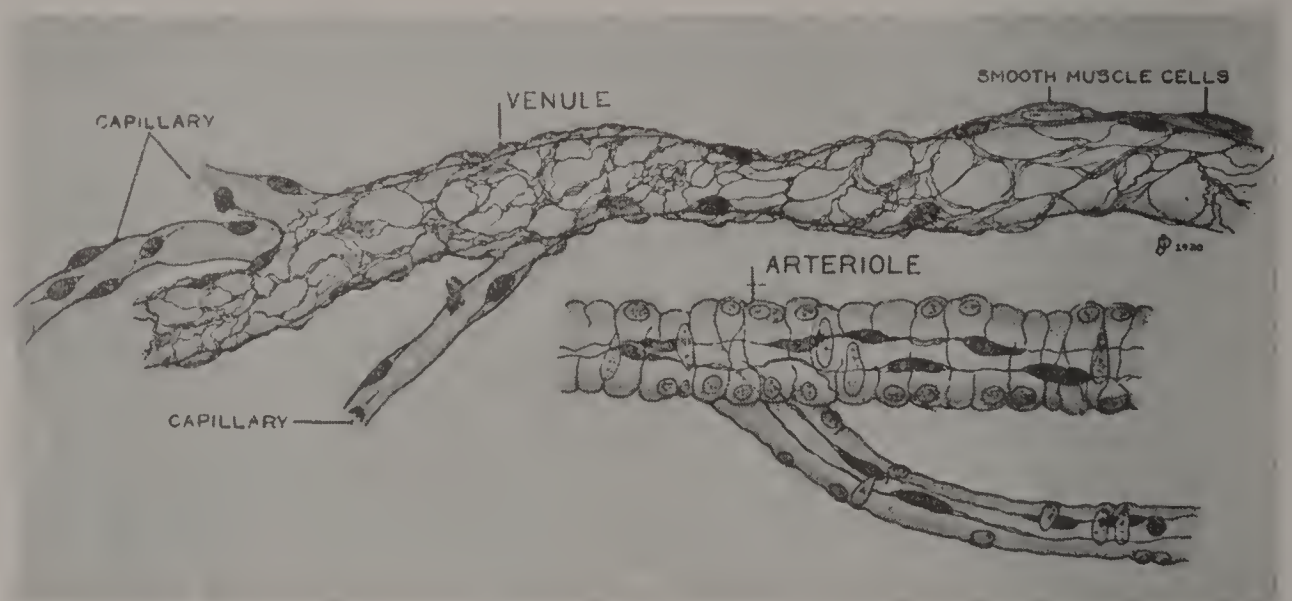


FIG. 9.—Schematic representation of the relation of the muscle cells and connective tissue about the arterioles and venules. (*Hooker and Sabin*)

Towards the periphery and along the arteries, there is a gradual decrease in the size of the lumen and in the thickness of the vessel wall. This attenuation goes hand in hand with the diminution in connective tissue elements. The smallest arteries are composed of an endothelial lining (intima), a layer of connective tissue fibers and a layer of muscle fibers. In the arteriole there occurs an elimination of the connective tissue layer between the endothelium and the muscle fibers. The arteriole is, therefore, made up of muscle and endothelium alone. Towards the periphery, the arterioles subdivide and become diminutive; with this, the muscular layer is attenuated gradually until but the simple endothelial capillary tube is left.

The capillaries in their turn give way to the venules, a transition that is accomplished by the addition of a connective tissue layer. This antedates the inclusion of muscle fibers. Thus there is a sharp structural contrast between the arteriole and the venule. The arteriole is characterized by the muscle substance intimately overlying the endothelial tube, while the venule exhibits connective tissue in the same situation (Sabin).

This morphologic distinction is depicted in Fig. 9 where the differential structural disposition of muscle cells about the arterioles, and of connective tissue on the venules is evident.

THE ARTERIES

Arteries of medium size offer rather typical pictures in exemplification of the muscular variety and may be briefly described here.

In cross section the intima has a folded appearance directly applied to the plication of the internal elastic membrane. The latter presents a striking corrugated line marking the external limit of the inner coat. The endothelial cells are so thin that they are recognizable mainly as projecting nuclei. But between the endothelium and the elastic membrane there is a fine layer of connective tissue and elastic fibrils.

The media is composed of circularly distributed muscle fibers interspersed with elastic tissue plates, whose presence can be intensified and brought to view by appropriate elastic tissue stains. The external elastic membrane, the middle and external tunics, are separated by a distinct layer.

The adventitia is of varying thickness and is relatively larger in the medium sized arteries than in the larger ones. It is composed of fibrous tissue and elastic fibers, contains the vaso-vasorum, and main lymph channels of the vessel wall.

The Structure of the Arteries in Embryonal Development.—Two types of arteries have been distinguished, the elastic and the muscular types. Of the

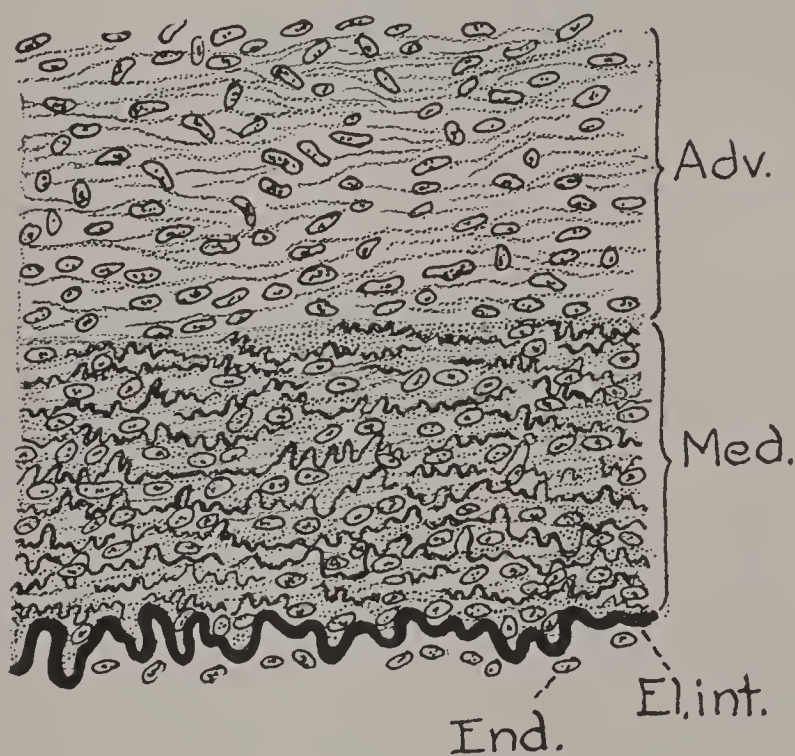


FIG. 10.—Transverse section of the aorta of an embryo (about the middle of embryonal life); numerous elastic fibers in the media; none in the adventitia. (*Aschoff*)

former the aorta is an example, of the latter, the arteries of the extremities—such as the brachial. For a correct understanding of what is normal and what constitutes atherosclerotic or arteriosclerotic change, the normal alterations in the arteries through embryonal life and during the first 2 or 3 months of extrauterine life must be borne in mind.

About the fourth month in both types of vessels differentiation in the intima, media and adventitia occurs, with simultaneous development of muscle fibers, elastic tissue and fibrillar connective tissue.

The Elastic Type.—The aorta (Fig. 10) as an example, in the fourth month of the embryo presents an intima made up of endothelium, a relatively broad elastica interna with rather regular folds. The media includes about ten rows of nuclei, containing numerous elastic lamellae interspersed

between these. Towards the adventitia these are absent, although no distinct membrane demarcating the boundary can be discerned. Here the adventitia is broader than the media, and made up of connective tissue.

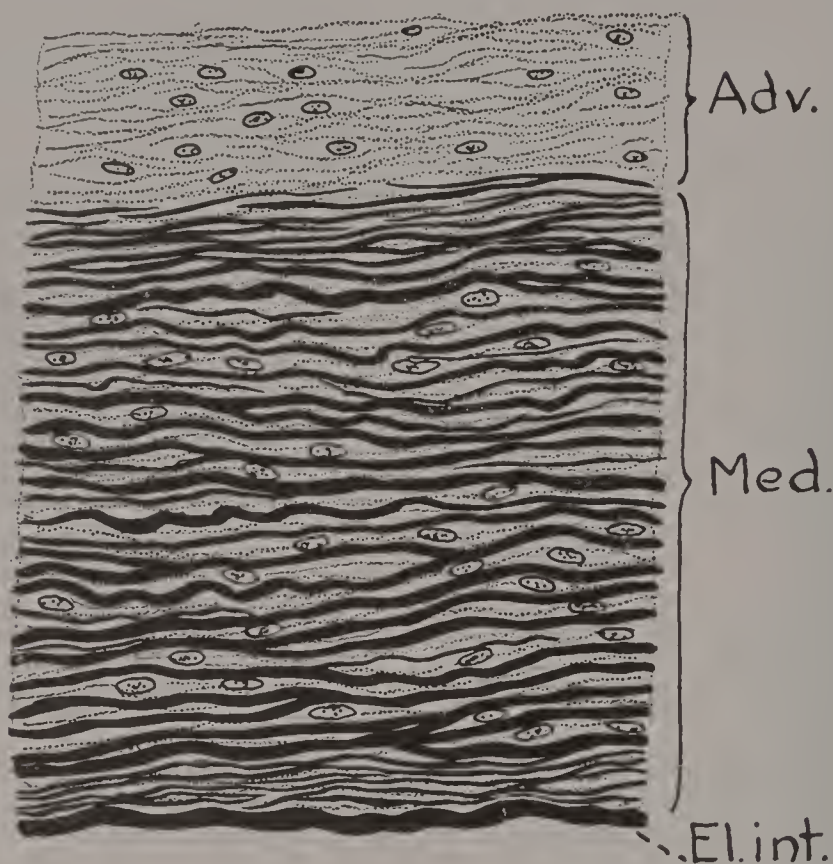


FIG. 11.—Transverse section of the aorta of an embryo taken at the end of embryonal life.
(Aschoff)

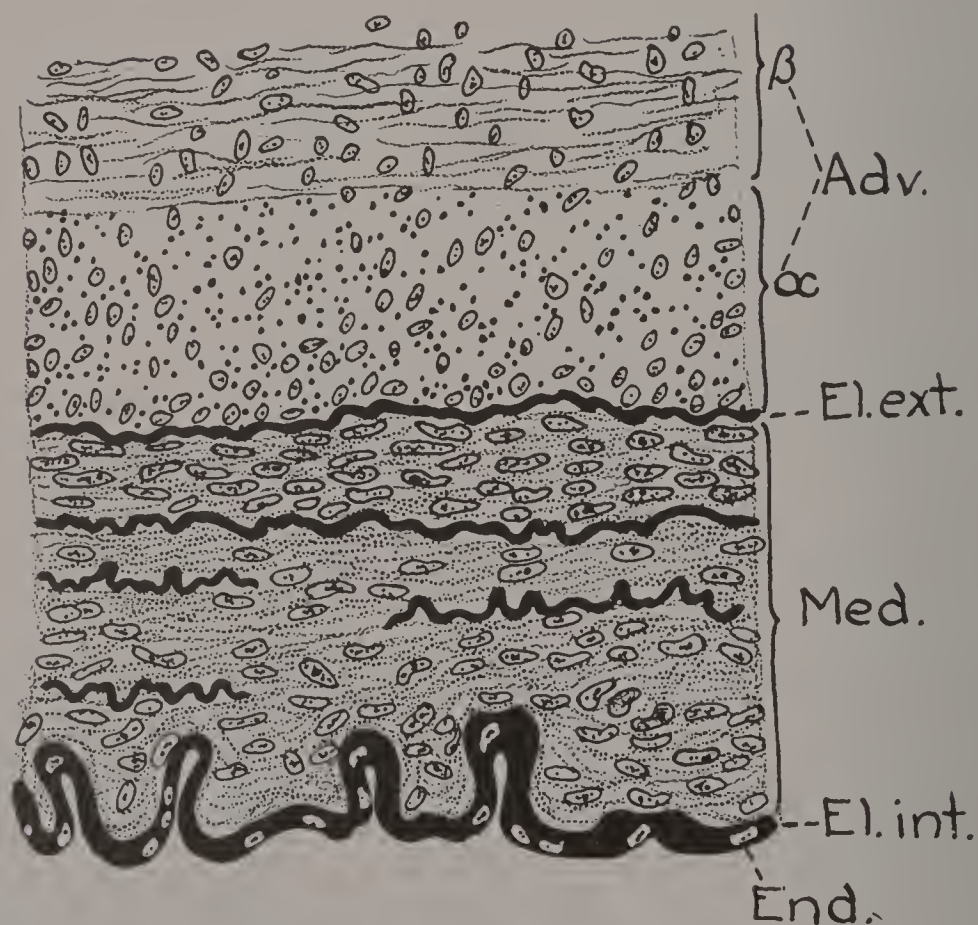


FIG. 12.—Section of the brachial artery of an embryo taken at the end of embryonal life.
(Aschoff)

The muscular type of artery, as the brachial at 6 months, has a well developed endothelial layer and elastica interna. The media contains muscle cells arranged in a more orderly fashion with a very few interspersed

elastic fibers. The adventitia and the media are distinctly separated through an elastic membrane. The adventitia is different being characterized by the appearance of two laminae, the inner one disposed longitudinally, the external more or less circularly and irregularly. Furthermore, longitudinally coursing elastic fibers in the inner portion of the adventitia appear at this stage in a rather characteristic fashion, for such a layer is absent in the elastic type of vessel.

The Arteries Shortly before Birth.—Late in the embryonal stage the differences between the muscular and elastic types are more striking. In the aorta, besides the general enlargement, the absence of plication is a feature. In the media the marked development of the elastic membrane is prominent, the muscle cells being relatively few in number. The elastica externa is here also absent. The adventitia becomes relatively narrow, being made up of connective tissue without elastic elements (Fig. 11).

In the brachial artery (muscular type) the internal elastic membrane becomes thicker, being regularly folded on section (Fig. 12). In the media the muscle cells are prominent in number and spindle shaped, particularly in the outer layers. The elastic fibers have multiplied in the media, although not so intensively as in the musculature. In the adventitia, however, the elastic fibers have hypertrophied and are disposed in a longitudinal direction, being in far greater abundance here than in the media. The separation from the media through the elastica externa here, too, is noteworthy.

In short, the differences in and during the embryonal development of the two types of vessels are: The appearance here and there of connective tissue layers in the intima of the vessels of the elastic type with marked development of the elastic membrane; in the arteries of the muscular type, the media and musculature are prominent, as are also the elastica externa and the longitudinal elastic fibers of the adventitia.

The Arteries in Extrauterine Development. *The Elastic Type.*—Three layers in the intima have been described in the elastic arteries of children¹ (Fig. 13). On cross section the elastica interna is seen to be split into two or three lamellae, that frequently reunite. Here and there, are interruptions that probably indicate openings in the lamellae. Adjacent and on the inner side are numerous longitudinal elastic fibers, including a similar distribution of cells. Then there is a circular layer of elastic fibers and finally an innermost delicate layer of connective tissue, upon which the endothelial cells are deposited. Jores has called that layer, which lies against the elastica interna, an elastic muscular layer, the next one of hyperplastic thickening of the intima, and the innermost, the connective tissue layer.

The growth and development of the musculo-elastic (as well as the hyperplastic layers) attain their maximum at the climax of bodily development, namely between the twenty-fifth and thirtieth years. The connective tissue coat develops more tardily, possibly after the thirtieth year. These three layers may attain considerable thickness at an age when morbid changes in the vascular system are not as yet to be expected. It is only when the hyperplasia becomes extensive (especially of the connective tissue coat) that the so-called sclerotic process is said to begin.

For our studies of the peripheral circulation we are concerned especially with the following type.

The Muscular Type.—Characteristic for these arteries in their further development, is the relative marked hypertrophy of the muscular layer

¹ Aschoff, Description given as applying to ages of 1-4 years.

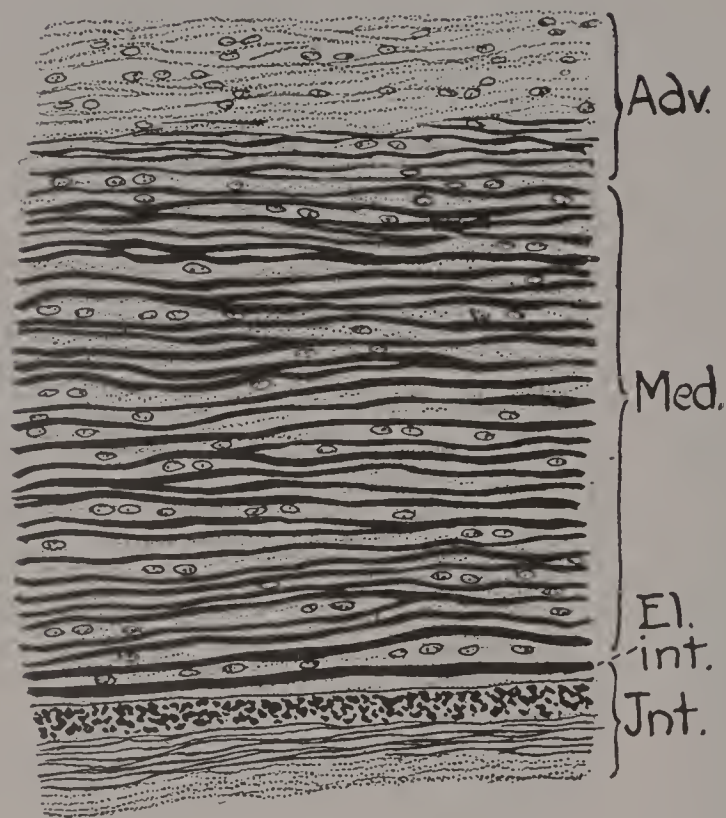


FIG. 13.—Cross section of the aorta of a child 3 years of age; in the intima three layers; the external cut transversely being a musculo-elastic longitudinal layer; the middle portion a hypertrophic elastic layer; the innermost one of very delicate connective tissue belonging to the normal period of growth. (*Aschoff*)

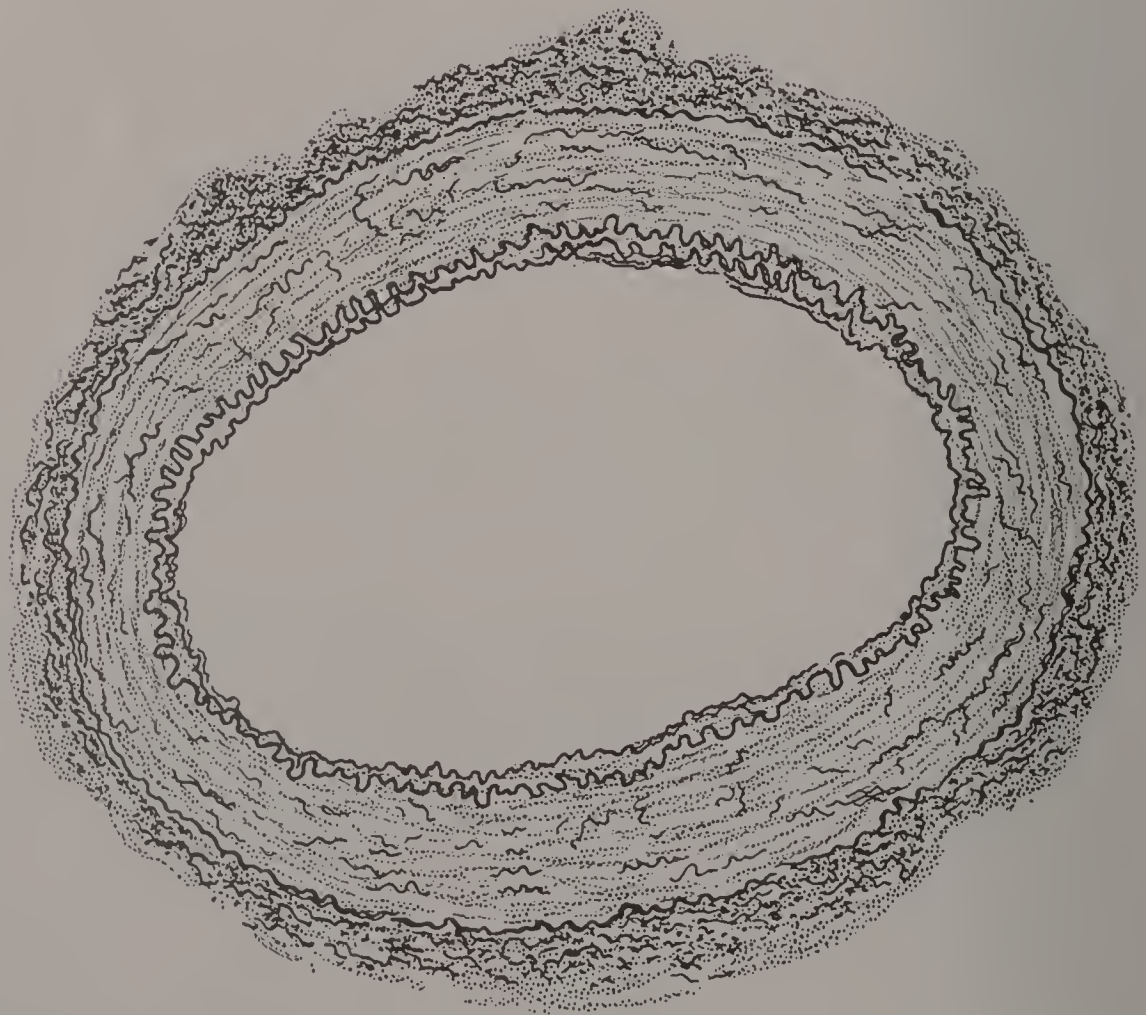


FIG. 14.—Cross section of the radial artery at the climax of its development (third decade); slight development of a hypertrophic elastic coat in the intima, belonging to the normal period of growth. (*Aschoff*)

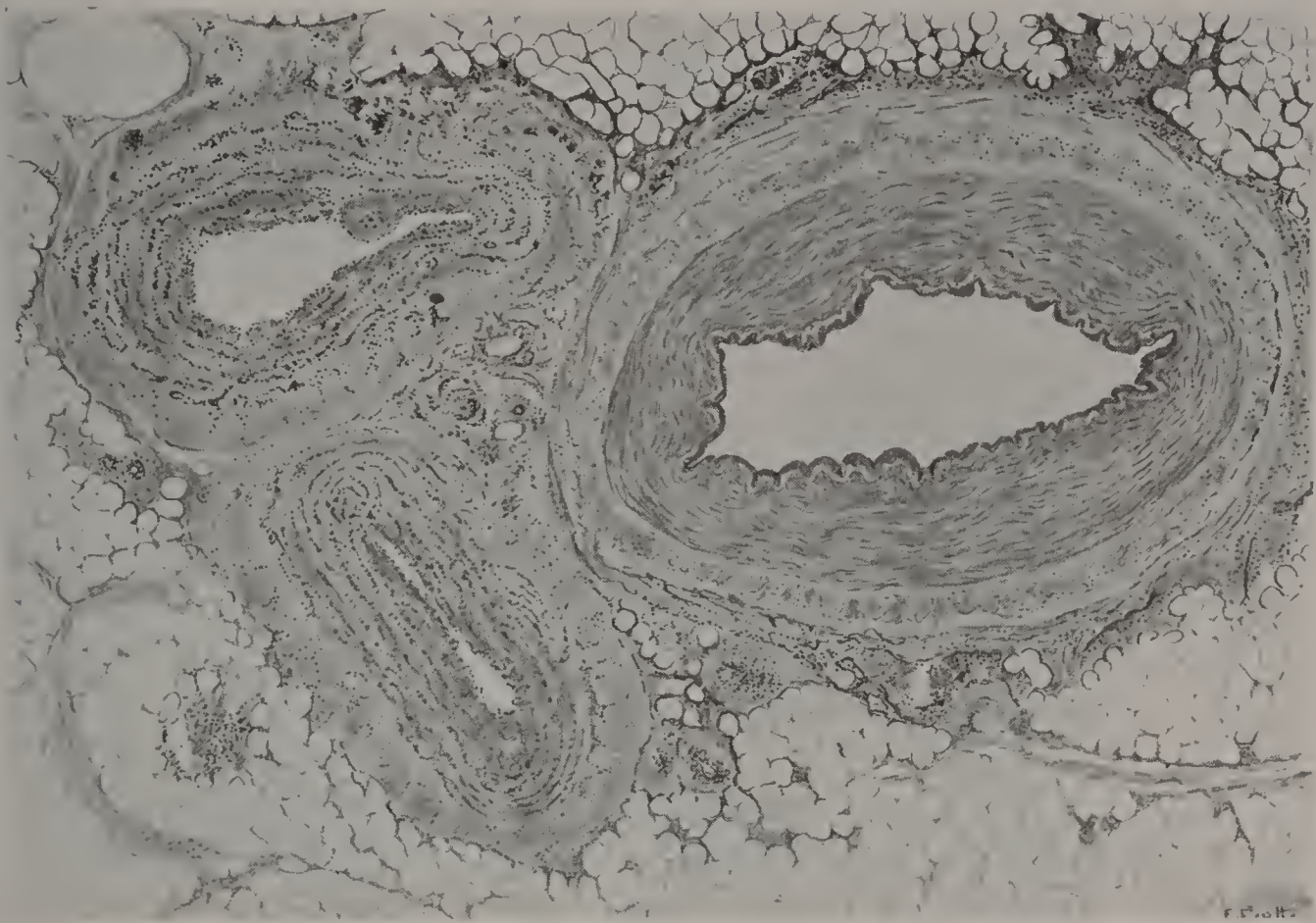


FIG. 15.—Normal posterior tibial artery and vein in cross section. Here there is but the slightest degree of thickening of the intima in places.

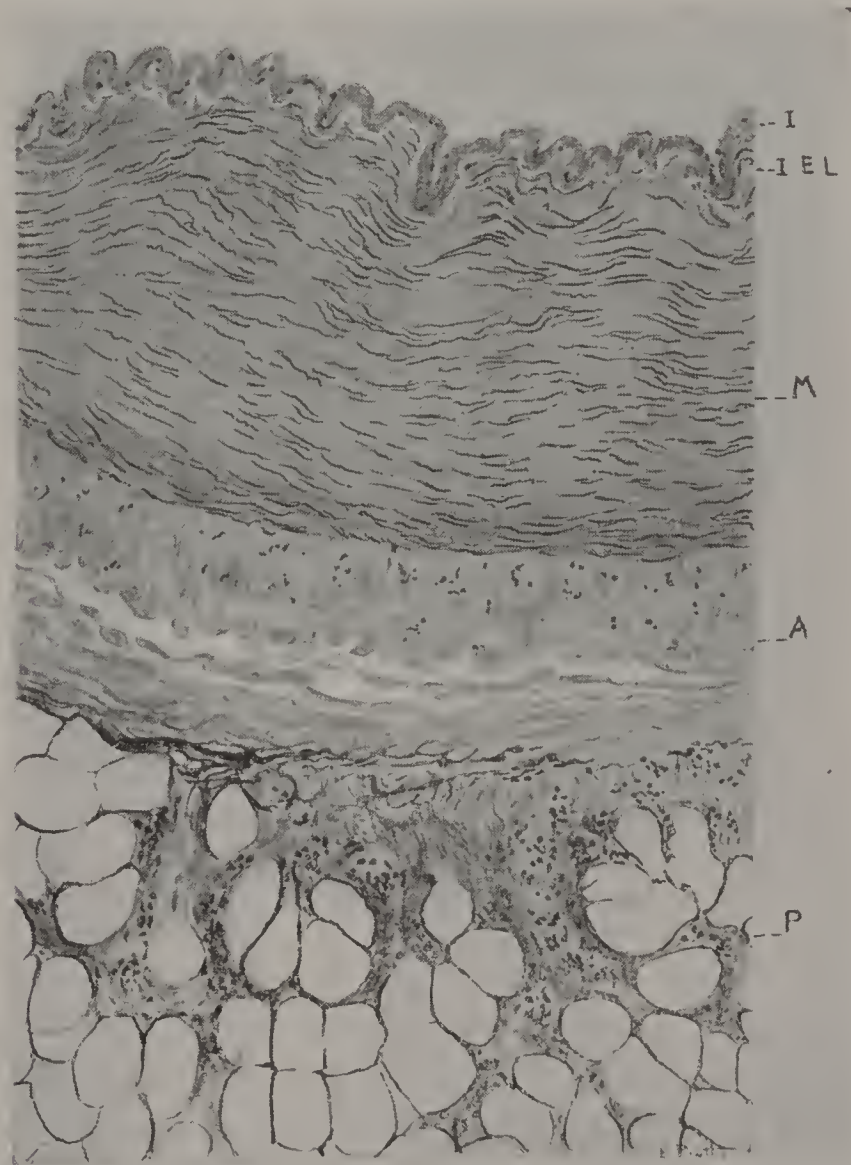


FIG. 16.—Normal posterior tibial artery; muscular type (high power).

(Fig. 14). As far as the adventitia is concerned, it is believed that the longitudinal elastic fibers undergo a marked increase during the early years. On the other hand the inner elastic layers do not develop that marked differentiation and increase that are noticeable in the larger arteries of the elastic type (the aorta and carotid). The hyperplastic intimal layer may be slight in extent, but the musculo-elastic longitudinal layer is absent or but little marked. In the adventitia, on the other hand, the elastic fibers are exceedingly prominent.

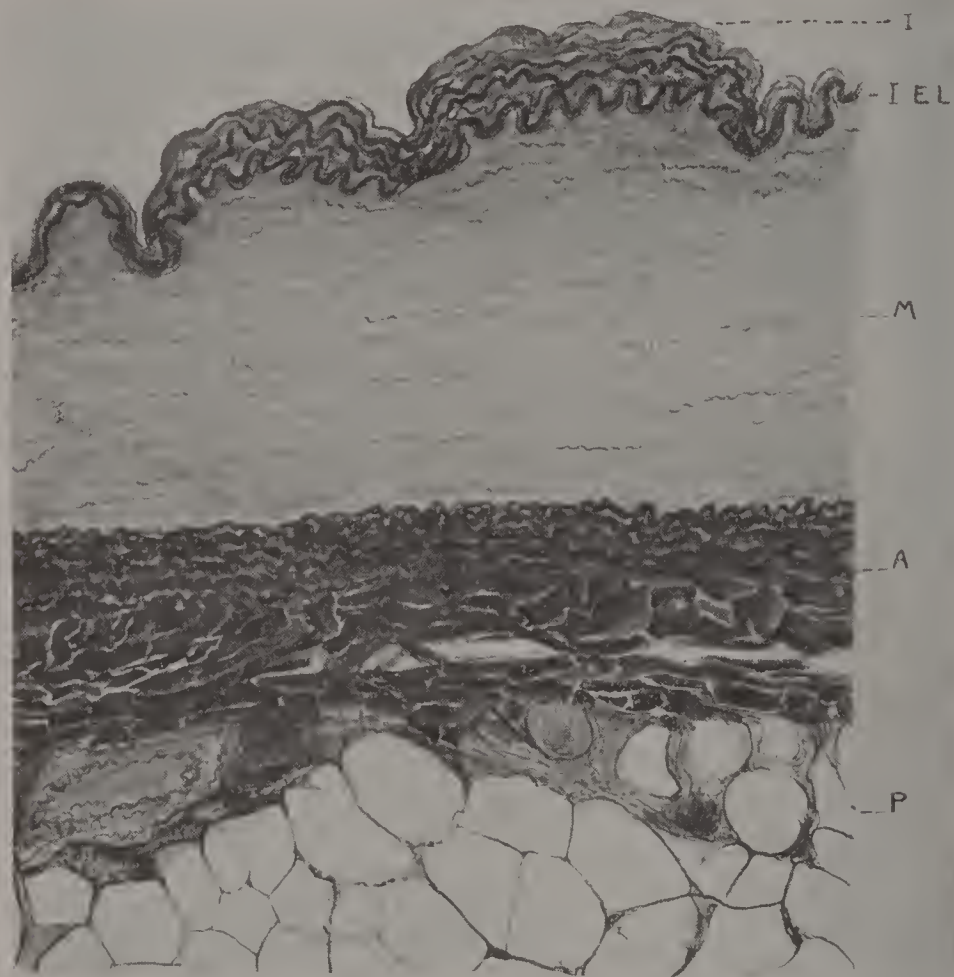


FIG. 17.—A, Elastic tissue stain of a normal (posterior tibial) artery showing early thickening of the intima (possibly early arteriosclerotic thickening) with reduplication of the intimal elastic fibers; IEL, internal elastic lamina; M, muscular coat (media); A, adventitia; P, perivascular fatty connective tissue.

Figs. 15 and 16 illustrate a “normal” posterior tibial artery and vein. For purposes of orientation and comparison with the lesions to be described in later chapters, it may be well to point out the following characteristics; the adventitia is narrow and loosely bound with the surrounding connective tissue as well as with accompanying veins; the circular muscular layer is relatively well developed (media) and evidences great dearth of vascular elements; the intima is narrow except in those zones of slight thickening that may be regarded as within the normal, or insufficient to be designated as arteriosclerotic. Thickening of the intima within the physiological limits is depicted in Fig. 17.

A somewhat more marked example of the effects of hydrostatic and mechanical (perhaps also toxic) stresses on the development of the peripheral arteries is depicted in the sections taken from the dorsalis pedis artery of an adult. In Fig. 18 we have an excellent illustration of the relation of the artery to the veins, the absence of vascularization of adventitia and media so characteristic of the normal. In the discussion of the inflammatory

diseases of the arteries (arteritis, periarteritis and thrombo-angiitis, etc.) and of the intravascular thrombotic processes, it will be seen how penetration of these coats with new formed vessels may occur; and how in some of them, the adventitia and the relation of the artery to its accompanying veins becomes altered.

In the section of the artery, too, when seen under greater magnification (Fig. 19), the hypertrophy of the middle coat is in evidence. Slight proliferative changes in the intima, also, mark the transition of a normal artery into the early stages of arteriosclerosis.

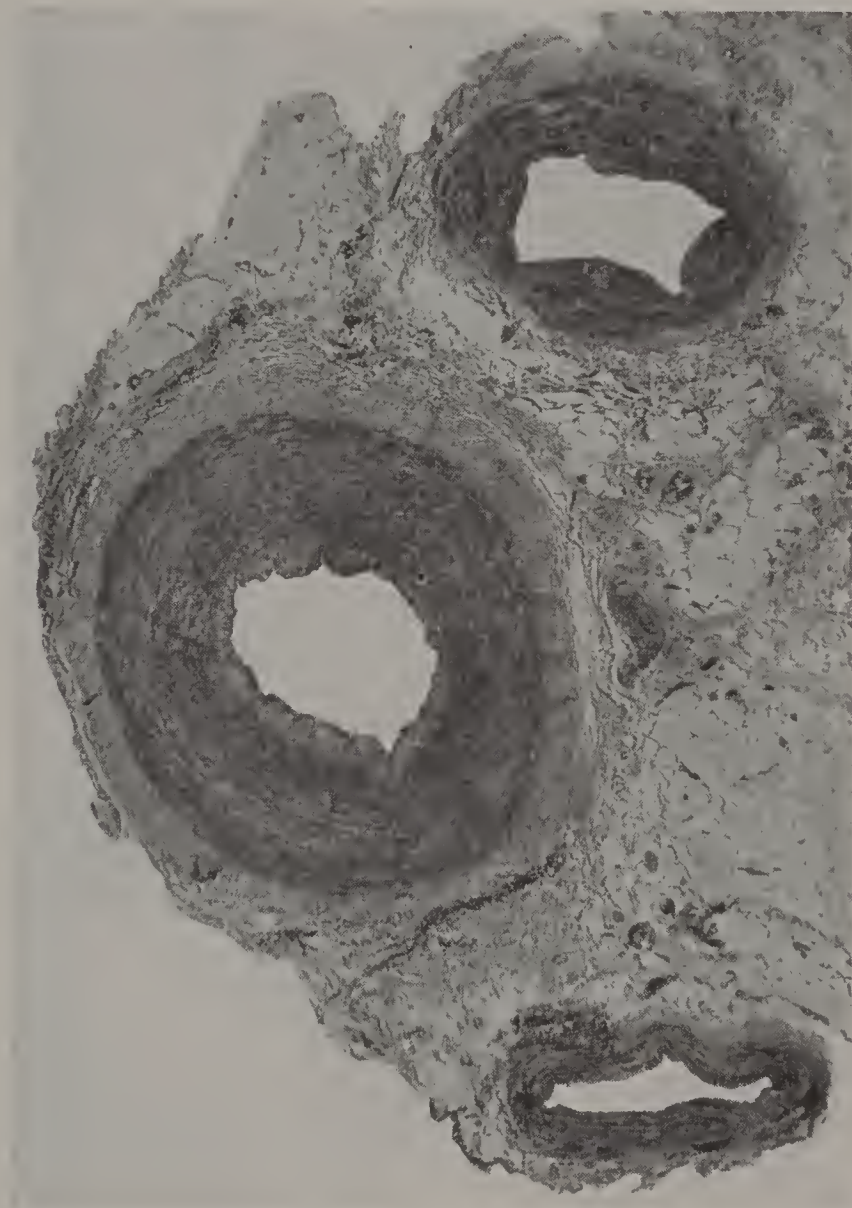


FIG. 18.—Low power transverse section of almost normal dorsalis pedis artery and veins, showing slight hypertrophy of the media and beginning thickening of the intima; the avascular condition of the media and adventitia are well shown, and the loose connection between artery and veins.

The Senile Changes in the Arteries.—Aschoff, Marchand, Jores and others point out that the first senile changes are the hypertrophy of the musculo-elastic longitudinal layers of the intima (Fig. 20). There is no sharp differentiation between the antecedent normal development and the subsequent pathological thickening. It is only the proliferating connective tissue that signalizes a distinct senile change. This connective tissue is deposited between the elastic fibers of the hyperplastic layer, occupying there a dominant position. Besides, it is laid down as a strong connective tissue lamella upon the old intima. It is often difficult to differentiate between normal physiological thickening and senile sclerosis. In the aorta

and larger vessels there is usually associated fatty degeneration. Jores believes that this process begins in the outermost layers of the intima, that is, in the musculo-elastic longitudinal coat (Fig. 21). Later fatty degeneration and calcification may take place; and coincidentally or subsequently reactive and degenerative processes in the new-formed intimal layers, with thrombotic deposits in the lumen and organization.



FIG. 19.—Cross section of slightly hypertrophic dorsalis pedis artery showing slight intima hypertrophy. The intima is somewhat thicker than normal, but avascular; adventitia normal (higher magnification of Fig. 18).

In the elastic type of arteries (aorta) the changes in the media are less intensive. Atrophy does occur and elastic lamellae and muscle fibers disappear. Although microscopically evidenced, the macroscopic destruction of the media is relatively slight. Streak-like areas of fatty degeneration in the middle coat and very fine lime deposits do appear.

In the arteries of the extremities (muscular type) the change in the media and the calcification are noteworthy, and preponderate over the intimal changes. When the arteries of this type in the extremities undergo calcific

alterations, the earlier manifestations thereof will be represented by fatty degeneration especially pronounced in the media; the lime deposits follow (Fig. 22). Bone formation as a sequel is not uncommon.

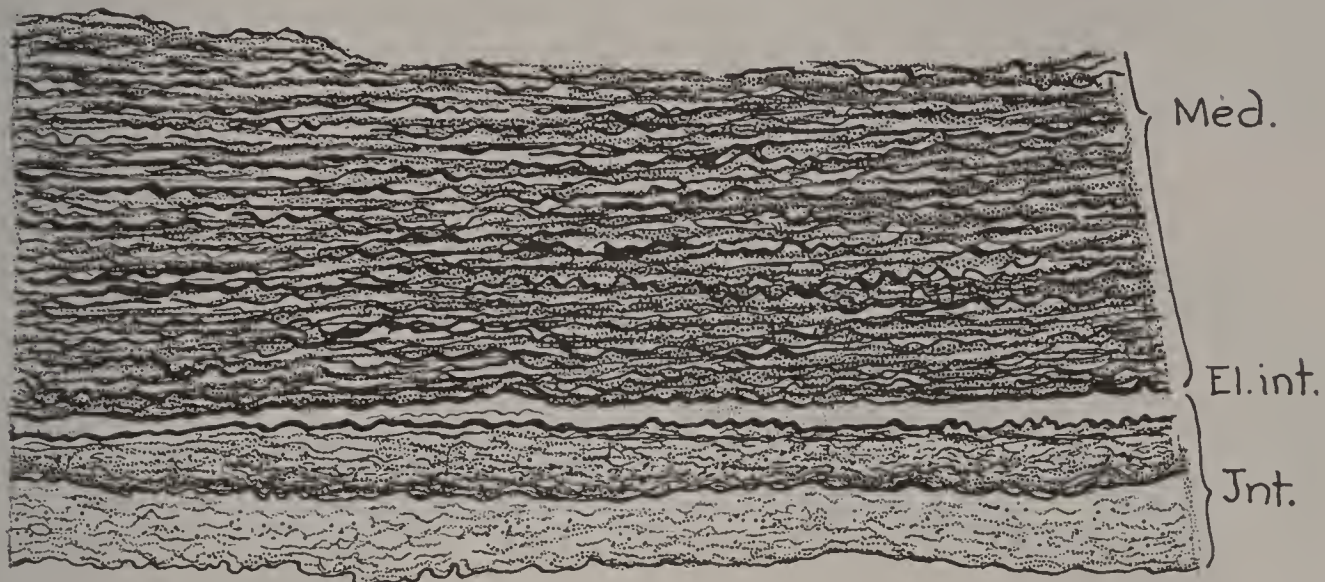


FIG. 20.—Cross section of the aorta at the time of complete development (third decade); in the intima still distinct division into three layers, but with hypertrophy of the connective tissue. (*Aschoff*)

The intimal lesions in the peripheral vessels are also of importance and are essentially represented by the endarterial thickening through connective tissue proliferation. Fatty degeneration is not so characteristic here. According to Mönckeberg the changes in the media of the arteries of the extremities preponderate numerically over those in the intima.

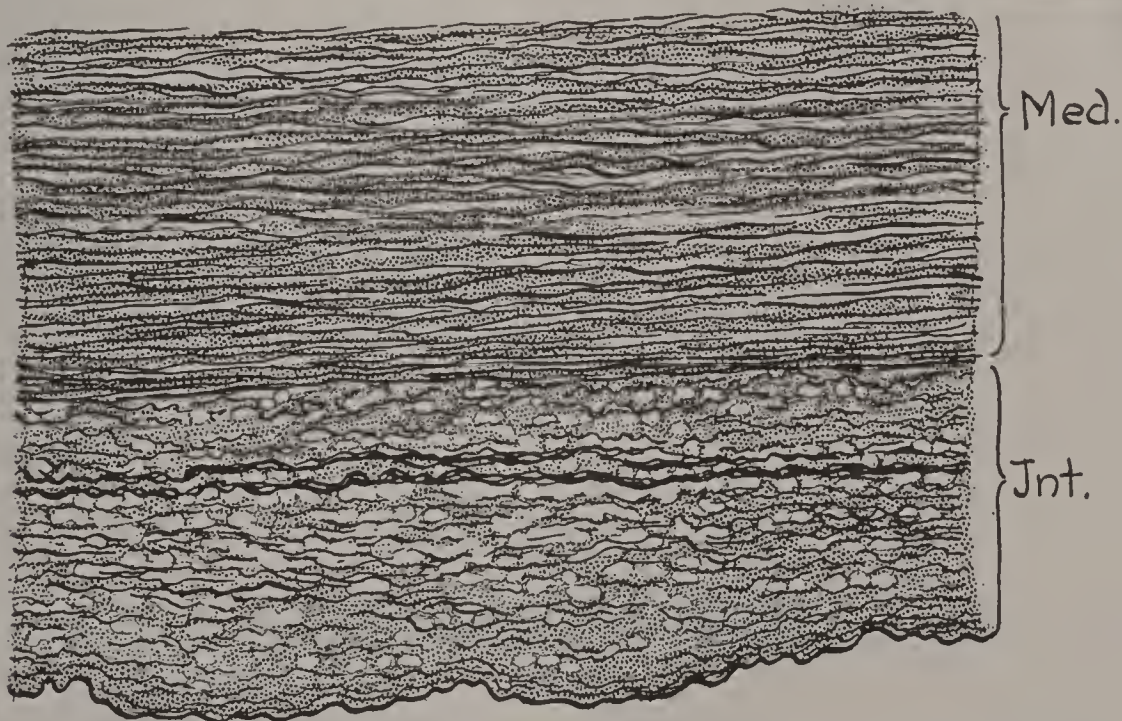


FIG. 21.—Transverse section of the aorta with beginning atherosclerosis at the end of the fourth decade; marked connective tissue hypertrophy and fatty degeneration of all three parts of the intima. White areas are those of fatty degeneration. (*Aschoff*)

The Development of the Arteries and Their Subsequent Pathological Changes.—It is rather interesting to observe that those elements of the arteries that exhibit their most profound development late in embryonal life, and in the early years of extrauterine growth, also suffer the greatest pathologic alterations in atherosclerosis. If the latter be regarded as a disease of deterioration, functional stresses (or overactivity) must partici-

pate in the resultant lesions. So in the larger arteries of the elastic type, by virtue of the arterial pressure and its constant variations and the pulsative forces, extensive and distensive stresses must needs exert longitudinal and lateral tension on the elastic element of the intimal tubes. With this comes a tendency to tearing in the longitudinal, as well as in the circular direction. Such factors have been regarded as playing an important rôle in the consequent pathologic alterations.

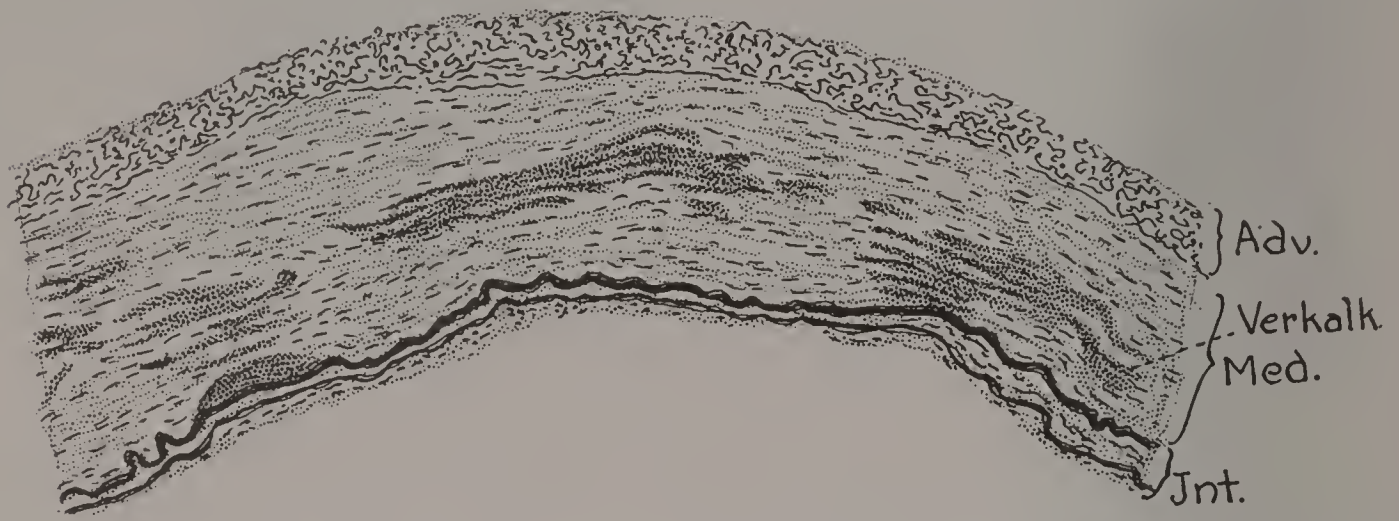


FIG. 22.—Transverse section of the femoral artery with beginning arteriosclerosis at the end of the fourth decade; in the media areas of calcification. (Aschoff)

In explanation of the precocious development of atherosclerosis the question has been raised as to what influence toxic elements (*e.g.* alcohol, nicotin) may have upon the elastic elements of the arteries; or what rôle an acquired predisposition on the part of the elastic elements through previous infectious diseases may play. In the muscular type of vessels the muscle fibers would necessarily suffer greater strain through the arterial pulsations and excessive dilatation and contraction. Changes in blood pressure and in the blood stream too, have been regarded as of importance. The special demands of overacting musculatures of the extremities; the functional demands of the peripheral arteries; the increased tension resulting from difficulties in the capillary flow; the modifications due to vasomotor influences—all these are believed to be motivating elements.

CHAPTER IV

THE VASOMOTOR NERVOUS SYSTEM

It is a perplexing but nevertheless an interesting clinical fact that many of the objective symptoms resulting from organic closure of the larger arteries and veins of the extremities can be easily confused with manifestations of altogether different etiologic significance. These are in the main nutritive and trophic derangements on the one hand, and circulatory and vasomotor on the other hand. And, therefore, it behooves the clinical observer to be able to discriminate between atrophies or lesions of the skin, and other tissues that result from circulatory impairment (purely trophic or nutritive), and similar alterations due altogether to nerve influences (neurotrophic). And so, too, disturbances in the vasomotor mechanism may cause

phenomena simulating closely those of hydrostatic and mechanical vascular origin.

A loose concept obtained by a cursory reading of text books on neurology concerning neurotic trophic lesions should be supplanted by a systematic and detailed study of the anatomy and physiology of the sympathetic system, and what is known concerning the neurotrophic, and neurosecretory paths. For the sake of completeness, therefore, the salient features of the anatomy and physiology of this portion of the nervous system are described in detail.

Course of Vegetative Nerve Fibers.—The cerebrospinal motor fibers that enter the sympathetic system end in branches about the sympathetic cells, but never directly in vessel walls or other peripheral localities. Their course is of varied length, some terminating in the nearest ganglion cells— in the corresponding ganglion of the ganglionic cord, others traversing several ganglia; still others continuing until they reach the most peripherally situated ganglia. It is most probable that all sympathetic cells are influenced through motor fibers emanating from the cord; on the other hand, the motor ganglionic fibers of the sympathetic, never act upon other ganglionic cells. Even these fibers are of different length ending at points near or far from their source.

Medullated fibers originate in the central nervous system with their cells in the gray substance, travel in a cerebral or spinal nerve, or with several of these in a cord to a sympathetic ganglion. This *preganglionic* cerebrospinal fiber ends in a ganglion in that its dendrites surround the sympathetic cell in a dense network or in sparser distributions. The sympathetic cell in many instances sends a non-medullated axis cylinder to the peripheral tissues (the postganglionic fibers of Langley) where this terminates without cellular interposition. *The central precellular fibers never come into contact with the peripheral tissues, but influence only the cells of the sympathetic system.* So also, a sympathetic, post-cellular fiber does not connect directly with a ganglion cell, but is in immediate communication with peripheral tissues, muscles, glands or intestine. A precellular fiber may traverse one or several ganglia before terminating.

The vegetative system may be subdivided into subordinate portions whose origins lie in various segments of the cerebrospinal axis. Five territories are recognized; first, centers in the corpus striatum; second, in the mid-brain; third, in the medulla; fourth, in the dorsal region up to the second and third lumbar segments; and fifth, in the region from the second to the fourth sacral segments (Fig. 23). The centers in the corpus striatum more recently recognized are shown in Fig. 24.

The mid-brain, bulbar and sacral systems are not infrequently spoken of as belonging to the *autonomic* or *parasympathetic* system, in contradistinction to the dorso-lumbar portion, called the *sympathetic* system.

It has been found that nicotin has a selective action on those ganglion cells in which an anatomical interruption of continuity takes place, with functional relaying of nerve impulses. Intravenous injection of nicotin as well as local application on a ganglionic node, cause transitory excitation followed by paralysis of the ganglion cells that lie in the relay station. Before nicotization, stimulation of a fiber of the vegetative system produces a certain irritative effect, irrespective of whether this excitation takes place before or beyond its entrance into the ganglion. Nicotin paralyzes the interpolated cell only, as that irritation of the preganglionic fibers is without effect; but the post-ganglionic fibers will respond as usual. *This action of nicotin is confined to the vegetative system.* The nicotin method, therefore, has been employed experimentally to indentify impulses that belong in the

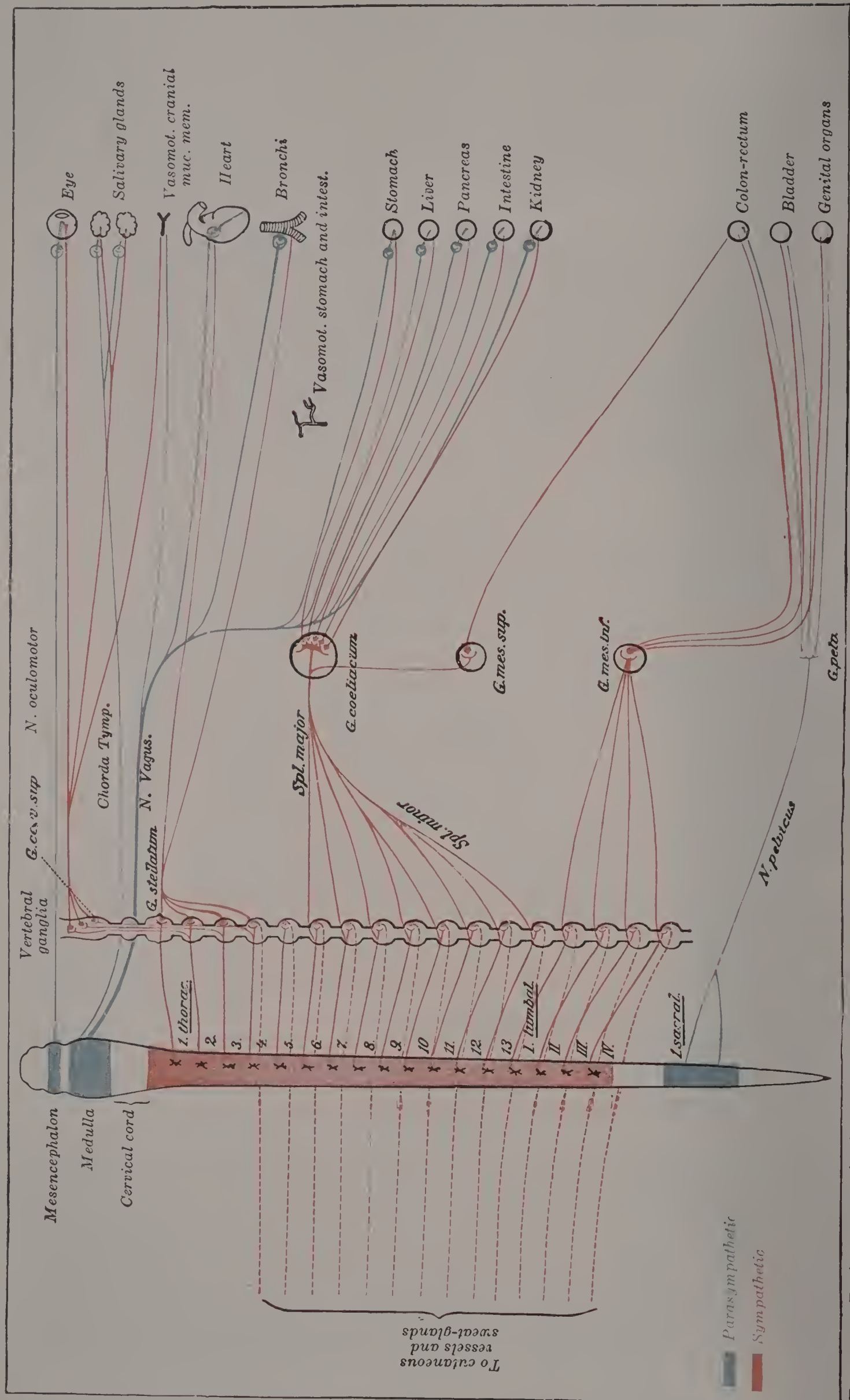


FIG. 23.—Red = sympathetic system. Continuous lines = preganglionic fibers. Dotted lines = postganglionic fibers. Blue = parasympathetic system. I, midbrain portion; II, bulbar; and III, sacral system. (Modified from Cassirer, Meyer and Gottlieb)

vegetative nervous system. It also permits us to decide as to whether a certain ganglionic node is an interrupting station for certain nerve fibers.

The *sympathetic system*, is composed of those spinal centers that lie in the lateral horns of the spinal cord, of the anterior roots emanating from these and leading to the ganglionic cord through the rami communicantes albi (Fig. 25).

Certain cells at the point of transition between anterior and posterior horns, sometimes designated lateral horns or intermedio-lateral tract have been regarded as the site of origin of the fibers leading to the gangliated cord. Jacobsohn¹ distinguishes a *nucleus sympathicus lateralis superior* extending from the eighth cervical to the third lumbar segment, and providing all the sources of the rami communicantes of the gangliated cord. In the parasympathetic system he describes a *nucleus sympathicus lateralis inferior* from the second sacral segment to the coccygeal; also a *nucleus sympathicus medialis inferior* located in the fourth lumbar segment and fusing with the above in the coccygeal region. All of these nuclei show interruptions in continuity throughout the various segments.

These rami are split up about the ganglia lying alongside the vertebral column. Here, the ganglia and their communicating fibers constitute the gangliated cord. The gray rami have their source in these ganglia, whence they course either independently (as in the case of the splanchnic nerve), or join the spinal nerve. The sympathetic system in a narrow sense is composed, therefore, of the spinal centers, the rami communicantes, the vertebral ganglia, the gangliated cord of the sympathetic and the peripheral sympathetic nerves. The upper limit of this system is the first thoracic nerve, and, in man, it extends downward, to the second or third lumbar segment. It is noteworthy that there are no sympathetic fibers arising from the cervical portion of the cord. In the cervical region, the gangliated cord has 3 ganglia; in the thoracic 11 to 12; in the lumbar 4 to 5, and in the pelvic 4 to 5 sacral and a coccygeal ganglion. The afferent fibers passing through the rami albi to the gangliated cord, arise from widely separated spinal segments. The efferent fibers, that is, the post cellular fibers are in rather close proximity, since in their further course they follow closely the spinal nerves in the immediate vicinity.

The superior cervical ganglion supplies the vessels and part of the glandular apparatus of the head, and part of the vessels of the brain, the dilator of the iris and Müller's muscle of the orbit. The stellate ganglion sends fibers to the thoracic viscera, and accelerating fibers to the heart. The rest of the gangliated cord supplies the muscles of the vessels of the extremities of the trunk, the muscles and glands of the skin, and the blood vessel muscles of the intestinal tract, of the lungs and intestines.

The anterior extremities receive their vasomotor fibers through the anterior roots from the 4th to the 10th dorsal nerves. According to Bayliss the vasoconstrictor nerves of the upper extremities leave the spinal cord in the anterior roots from the 3rd to the 11th thoracic nerves, whilst those for the posterior extremities are found in the 11th, 12th and 13th thoracic, and 1st to 3rd lumbar roots, in animals. The skin of the trunk in man derives its vasomotor nerves from the anterior roots of the dorsal and lumbar nerves. The lower extremities receive supply from the anterior roots of the last three thoracic and upper three lumbar nerves. It was formerly believed that only arteries received vasomotor fibers. It has been shown more recently, however, that the veins are also thus supplied.

¹ Jacobsohn, Abhandl. d. k. preuss. Akad. d. Wissensch., 1908.

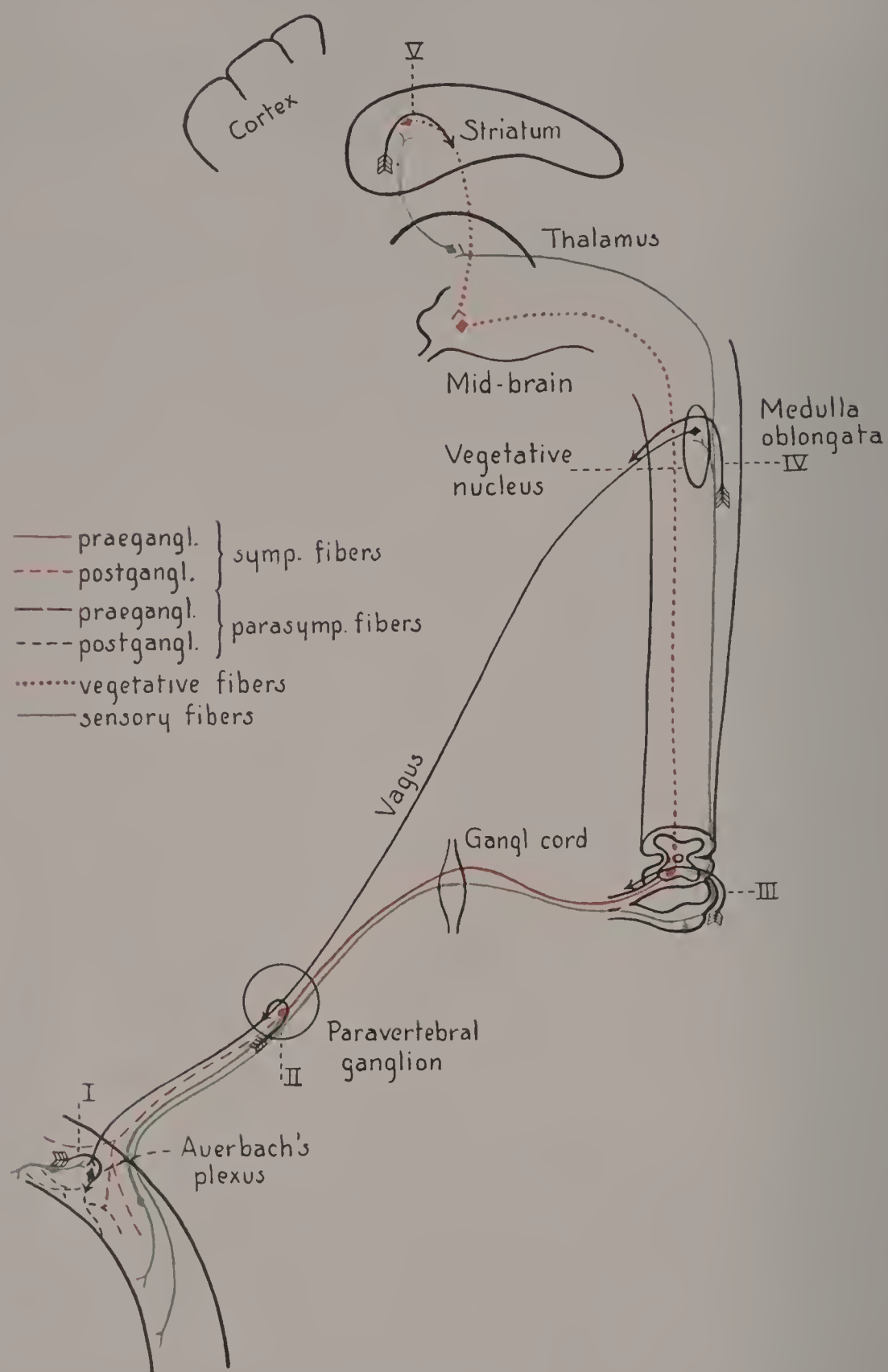


FIG. 24.—Reflex connections in the vegetative nervous system. Transference of an impulse at I into Auerbach's plexus; II, to the postganglionic sympathetic cell in the paravertebral ganglion; III, to the preganglionic sympathetic cell in the cord; IV, to the preganglionic parasympathetic cell in the medulla; V, to the vegetative cell in the corpus striatum. (*Modified after Dresel*)

Parasympathetic System.—We need merely to refer to this in a general way here, and point out to what extent this part of the vegetative nervous system deals with vasomotor impulses. The parasympathetic system is composed of the cranial and the sacral autonomic systems. Over the posterior roots of all of the dorsal and the upper lumbar segments there travel impulses, which serve to bring about vasodilatation and inhibition of perspiration in the territory of the trunk and the extremities.

That portion of this system, which is called the cranial autonomic system, does not concern us here, for its main portions constitute the oculomotor nerve, and ganglion ciliare, and the vagus. The sacral autonomic system is not involved in the innervation of the vessels of the extremity, but communicates with the pelvic plexuses, the *nervi pelvici*, and innervates the genitals and bladder (*nervi erigentes*).

But there is one portion of the parasympathetic system, which is said to furnish *vasodilator* fibers, and sweat inhibiting paths for the trunks and the extremities. The dorsal and upper lumbar spinal segments (Müller) not only give origin to sympathetic fibers for the vasoconstrictors, for the secretion of sweat and the pilomotors, but antagonistic impulses also travel herein. The parasympathetic system is included in the posterior roots and not in the anterior. Our knowledge of its functions, however, is not based upon morphologic data; relevant histologic information is not at hand, nor has the point of origin of these paths in the gray matter of the spinal cord been discovered.

Cerebral Vasomotor Centers.—Daily observations teach us that blood vessels are influenced by psychic states and therefore, by way of the cerebrum. The pallor of the face after fright, the blush after joy or erotic ideas are examples.

Cortical cerebral vasomotor centers for the various peripheral nerves were experimentally sought but without convincing results. Even the vasomotor disturbances after cerebral lesions, such as hemorrhage and tumors, and the vasomotor manifestations after cerebral injury are too little characteristic and uniform to allow of binding conclusions as to localization. There are no certain data at hand to prove the existence of special vasomotor centers in the cortex. In a search for such centers elsewhere in the brain, physiological experiments have brought to light that vegetative functions may indeed be influenced from a very small cerebral territory. It is believed that the cerebral vasomotor center resides in the mid-brain, in the optic thalamus and in the gray matter of the third ventricle.

The removal of the cerebrum in a dog is not followed by any permanent functional vascular derangement. There are, however, localities in other portions of the brain that may be shown to affect the vasomotor nerves. Studies on hyperthermia have demonstrated that special modes of stimulating the corpus striatum lead to elevation of temperature ("heat puncture" of the German authors). So also, ablation of the anterior and mid-brain of rabbits destroys the function of heat regulation, while exclusion of the anterior brain alone is not followed by this result.¹ Karplus and Kreidl demonstrated that a center for vasomotor innervation lies in the mid-brain, especially in the gray matter of the third ventricle. Not only are vasomotor phenomena dependent upon psychic changes and emotion, as manifested by external cutaneous phenomena, but distribution of blood in the organs of the chest and abdomen is affected thereby. Different parts of the body are not equally influenced by emotional states. The blood in the extremities seems to be diminished during intellectual work, with simultaneous increase of the blood content in the brain and abdominal organs.

¹ Isensch-Krehl, Arch. f. expér. Path. u. Pharmakol., Bd. 70.

Although the general tone of the vessels may be influenced through a circumscribed area in the third ventricle, it is a mooted question as to whether all vessel innervation has the same origin. Fluctuations in the tonus are not dependent on impulses traveling from the spinal cord or cerebral nerves in a centripetal direction alone. Activities in the neencephalon and excitation of the ganglion cells of the mid-brain following irritant effects of the blood itself, may also be effective.

In short, the region of the mid-brain, the optic thalamus, and the gray matter of the third ventricle, contain a center or centers from which sensory impulses are transferred to the vasomotor paths. This center admittedly controls the general tone of vegetative innervation and also the special reactions of the vessels. The fluctuations in tone of the centers are subject to and related to stimuli from three sources; firstly, through the spinal cord and centripetal cerebral paths; secondly, through psychic mutations in the cerebrum; and thirdly, by direct excitation of the ganglion cells in the mid-brain through special irritants in the blood.

According to Starling there is a small region of the medulla oblongata on each side of the mid-line in the neighborhood of the facial nuclei, that sends impulses. The normal impulses travel down the cord as far as the dorsal region, and then pass outward by the dorsal and upper lumbar nerves. These facts have been adduced from experimental section of the cord at various levels. A marked fall in blood pressure follows division on a level with the origin of the first dorsal nerve. Destruction of the above mentioned area in the medulla also causes immediate lowering of the blood pressure. These conclusions are further confirmed by the fact that, whereas stimulation of the anterior roots of the cervical and lower lumbar and sacral nerves has *no influence* on blood pressure, a rise of the latter can be obtained by stimulating any of the anterior roots from the first or second dorsal to the second or third lumbar.¹ That portion of the medulla concerned with the sending out of the tonic vasoconstrictor impulses, is spoken of as the vasomotor center. Here it is subject to and receives stimuli from all portions of the body, from the higher centers of the brain and especially from the viscera of the chest and abdomen through the vagi. And so, the sum of the impulses arriving at the center produces a state of average continued activity which is responsible for the maintenance of arterial tone and for the regulation of the arterial blood pressure.

Furthermore, paralysis of the vasomotors of the body, as manifested by dilatation of all the vessels of the trunk and extremities, follows section through the medulla oblongata or cervical cord, while this does not occur with an interruption made above the medulla and just below the corpora quadrigemina. Glaser rather doubts the existence of such a vasomotor center; but he is in accord with the view, that the vasomotor innervation travels through paths from the mid-brain through the medulla. Centers of limited function—local vasomotor centers—controlling the vessels of the brain, the salivary glands or the dilators of the facial skin territory, may according to this author reside in the medulla.

A few clinical observations corroborate the physiological deductions regarding the existence of chief vasomotor centers. A beautiful example of vasomotor disturbances induced by central lesions is the case of Rossolimo.²

A man 38 years of age had manifestations pointing to a growth in the right motor zone; namely, clonic contractions of the left side of the body and headaches; the left hand was cyanotic, edematous, and his temperature diminished. Operation disclosed a cyst, which was followed by a disappearance of the vasomotor manifestations. From this it was concluded by the author that the cortical vasomotor center lies near the motor area.

Oppenheim distinguishes a vasomotor form of Jacksonian epilepsy, and a vasomotor monoplegia, in which there are attacks of vasomotor disturbances in the arm and face of one side, with or without loss of consciousness, and

¹ Starling, E. H., *Principles of Human Physiology*, Phila., 1915.

² Rossolimo, *Deutsch. Ztschr. f. Nervenhe.*, 6, 1895, p. 76.

persistent vasomotor symptoms in the same territory, with only slight paresis and atrophy.

So also vasomotor changes with cyanosis are observed with the common forms of hemiplegia, with edema of the paralyzed side, symptoms that are not altogether to be explained by lack of function.

Subcortical vasomotor centers have been referred to the optic thalamus.

Little is known regarding vasodilator centers in the human. The cerebrum doubtless has an activating influence on the dilators, as evidenced in the vascular changes in the integument of the face.

From the center in the medulla oblongata the conducting paths of the vasomotor system pass to the lateral tract of the cord. Kocher in his study of vasomotor palsy after traumatic lesions of the vertebral column and cord, observed dilatation of the vessels and elevation of temperature of the paralyzed extremities. Such vasomotor phenomena, however, usually disappeared. In some cases pallor and diminution in temperature initiated the symptoms, these being irritative symptoms or evidences of incomplete paralysis of the vasomotors. Compression of the cord by tumors has been observed with vasomotor symptoms.

Recent Views on Anatomy.—While the descriptions that have preceded represent the accepted views prevailing for the last 10 years, a school of Continental investigators (Kraus, Brugsch and Dresel) has arisen that voices somewhat different anatomic as well as physiologic concepts.

According to Dresel there is a superior center of the vegetative nervous system in the corpus striatum. Subordinate to this there is a subthalamie center in the mid-brain which is in communication with the corpus striatum through the bundle of Forell and through the tinea lenticularis ("Linsenkernschlinge"). Nerves pass from the mid-brain to all points of origin of sympathetic and parasympathetic fibers in the mid-brain, medulla, thoraco-lumbar and sacral segments of the spinal cord. Whilst, according to Langley, only the thoraco-lumbar cord contains sources of origin for the sympathetic, and whilst parasympathetic fibers emanate from the other parts of the cord and medulla, it has been shown more recently that at least in the case of the dorsal vagus nucleus, both parasympathetic and sympathetic ganglion cells coexist (Brugsch, Dresel and F. H. Lewy). Furthermore, such a combination is believed to be possible in other parts of the central nervous system.

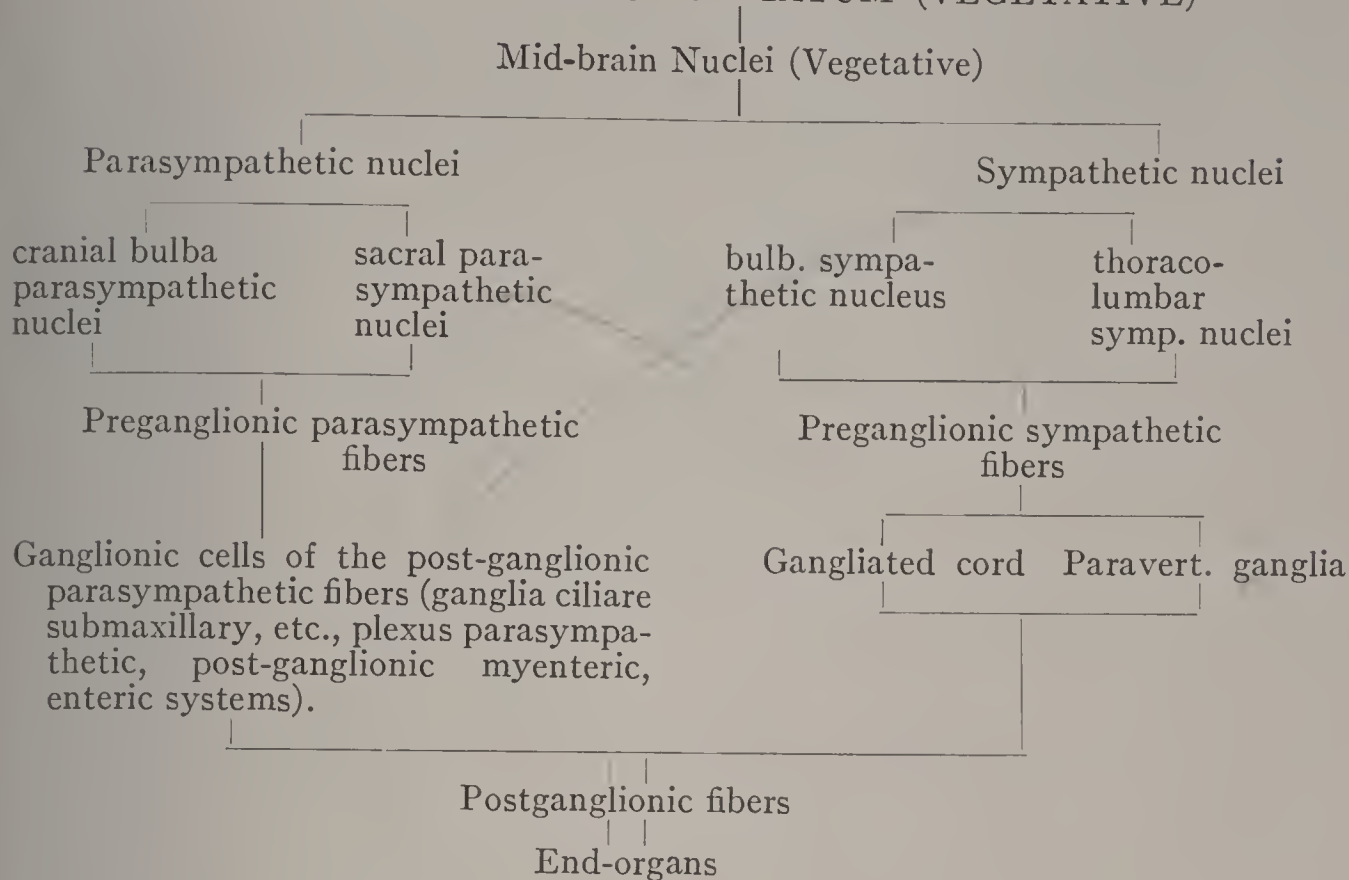
These parasympathetic and sympathetic nerves arising from the central nervous system, course in the following structures; in the ocular motor nerve, the corda tympani, the vagus, the white rami communicantes, the gangliated cord, and in the nervus pelvici, in the form of preganglionic, mostly medullated fibers. They pass to a second group of ganglion cells, namely the ganglion ciliare, ganglion submaxillare, the ganglia of the gangliated cord, the paravertebral ganglia and in the so-called enteric system. In the latter groups of cells, the interruption of all vegetative peripheral fibers takes place.

Parasympathetic and sympathetic fibers course as postganglionic fibers to their terminations. Most organs contain both parasympathetic as well as sympathetic fibers. According to Dresel the so-called enteric system¹ of Langley (which the latter regarded as an independent plexus, especially in the heart and in the intestinal tract) should more properly be included in the total mass of post-ganglionic cells; and this because it has been shown that these cells signify for the vagus (both anatomically and functionally) the very same thing that the cells of the ganglionic cord do for the sympathetic. Therefore, the following scheme has been suggested by this author.²

¹ Ganglion cell groups in the walls of viscera.

² This scheme has been obtained through the kindness of K. Dresel (Berlin) in a personal communication; to be published in *Handbuch d. Med.* Kraus u. Brugsch., 1922.

NUCLEI IN CORPUS STRIATUM (VEGETATIVE)



Spinal Vasomotor Centers.—There is no doubt but that there are segmentary centers for vessel innervation in the spinal cord. After a transverse lesion of the spinal cord, vasomotor responses are possible in the anaesthetic lower parts of the body. Reflex patchy rubor follows in the cutaneous area that is irritated with mechanical stimuli, such as needle pricks, provided that the corresponding spinal cord segment is intact.

Stimuli arising by way of the blood may also excite the spinal vascular centers. In asphyxia, even after section of the cord, an active vasoconstriction in the paralyzed part of the body is noted. This response is not obtainable if the spinal cord is destroyed.

The lateral horns are believed to contain the ganglion cell groups for vegetative function; and more correctly, in the intermediary zones between the anterior and posterior horns, where pyramidal or comma shaped ganglion cells control these functions. The cervical cord contains no such cells up to its lowermost portion. From the eighth cervical segment up to the lumbar, we find the lateral sympathetic nucleus. From this region emanate the vasoconstrictors for the face, the upper extremities, the trunk and the lower extremities. From the lateral and inferior mesial sympathetic nucleus that extends from the lowermost part of the lumbar cord into the sacral, the vascular nerves for the lower part of the intestines and for the inner and outer genitalia have their origin. The ganglion cells of the intermediolateral tract are aggregated into large groups in the middle and lower sacral cord. These completely fill the transitional zone between the anterior and posterior horns. Since the vasomotor nerves for the genitals, namely the nervus erigens or pelvic nerve arise from this segment, the conclusion is warranted that these cell groups are related to the vascular innervation of the sexual organs. It is impossible to differentiate, however, the cells that influence vascular innervation, and those which control the musculature of the pilo-erectors or the sweat glands. In syringomyelia and poliomyelitis vasomotor disturbances occur, such as vascular palsy, and lividity attributable to disease of the gray substance.

Vasomotor Paths in the Spinal Cord.—We still lack proof of the existence of special paths of conduction for the excitation of the vegetative functions. Clinical and experimental experiences warrant the conclusion that vasomotor impulses traversing each half of the spinal cord may arrive at both parts of the body. This explains the relative paucity of the vasomotor paralytic symptoms in the Brown-Séquard lesions. It has not as yet been proven that vasomotor paths course in the lateral tracts. The dominating vasomotor center in the mid-brain seems to conserve and regulate the general vascular tone. Perhaps qualitative alterations occur in the centers as the result of varied influences, and through these manifold reactions of the spinal centers ensue. It is not even definitely shown that the tonus is dependent upon the existence of certain paths, and the substantia gelatinosa or even the gray substance has been suggested as possible vehicle for the impulses. Some suggest that emotions may cause certain changes in the biotonus or in the general nervous excitability, because of the varied responses in depressive and sanguine states.

This tonus which controls the spinal cord is under the influence not only of the emotions, but also of sensory impulses. Various reflexes in the vegetative system, such as dilatation of the pupils or contraction of the tunica dartos follow severe pain impulses. In explanation of these phenomena it has been pointed out that all sensory paths cannot be in direct communication with all the vegetative centers in the spinal cord, or the medulla and mid-brain. Therefore, it may be accepted that impulses of sensory or of other nature may cause an alteration in the excitability of the gray substance of the spinal cord, with changes in its tonus. The latter in its turn influences the vasomotor cell groups.

In all probability the dominant tone of the spinal vasomotor centers is not transmitted through isolated paths, but propagated through the whole gray matter, and is modified through a multiplicity of influences, pain, temperature and the like.

The importance of the dominating vascular center in the brain and of the tonus influences that emanate therefrom, is shown in the experimental work on the effect of section of the cord on the heat regulating center. The latter is disturbed in proportion to the height of the spinal cord section, and depending upon the number of spinal centers that are thereby excluded from the influences of the cranial vasomotor center. High section of the cord in animals makes heat regulation impossible, and the animals die. Therefore, above the cervical cord there is a regulating center (vasomotor) that controls the tone of the inferior centers, but the manner of conduction has not as yet been discovered.

Relations of Spinal and Sympathetic Systems.—It must be remembered that all the paths between the spinal cord, ganglionic cord and peripheral nerves have not been definitely established. A reference to Fig. 26 will show the course of the known fibers in continuous lines, of the hypothetical fibers, in dotted lines.

The medullated fibers crossing from the cord into the sympathetic system arrive in the lateral horns; from here they pass through the anterior roots, into the peripheral nerves, making a sharp curve through the rami communicantes. Here they are medullated and constitute the ramus communicans albus. When the fibers arrive in the proximally situated ganglion of the sympathetic cord, they come into contact with the ganglion cells in parts, but their greatest portion continues cephalad and caudad in the internodal portion either to communicate with ganglia at other levels, or to enter the cervical sympathetic or splanchnic.

The non-medullated fibers course through the gray ramus to the peripheral spinal nerves where they supply the skin, vessels, sweat glands and piloerector muscles. However, there is also a communication between the gray ramus and the spinal cord (shown in the diagram in a dotted line) although their course has not been definitely established. Some fibers also pass to the thoracic and abdominal organs.

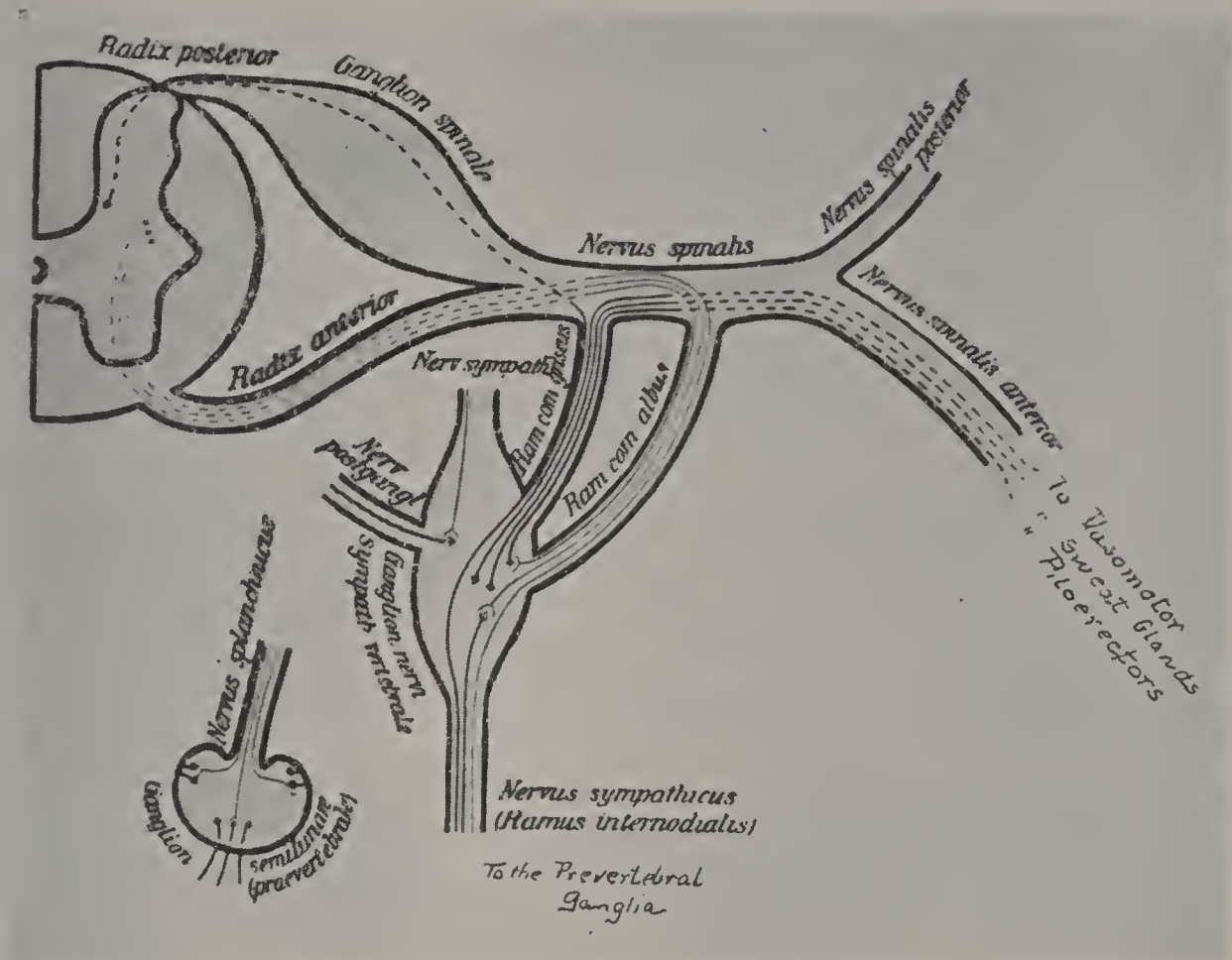


FIG. 26.—Scheme of the ganglionic and spinal communications of the sympathetic. Solid lines indicate definitely known paths; dotted lines still hypothetical. (Müller)

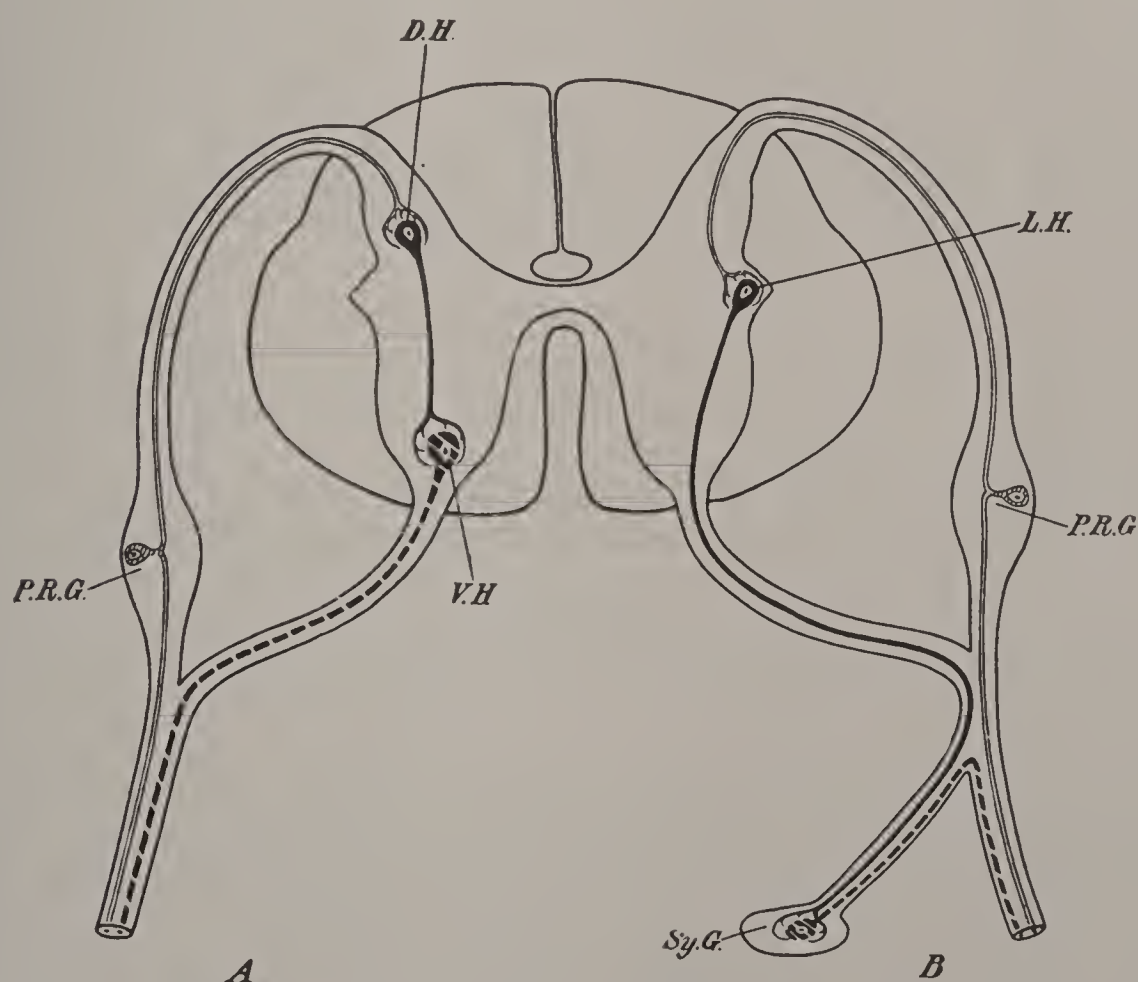


FIG. 26a.—Reflex paths in the cord. White, receptor neurones; black, connector neurones; dotted, excitor neurones; A, voluntary system; B, involuntary system; P.R.G., dorsal root ganglion; D.H., dorsal horn; L.H., lateral horn; V.H., ventral horn; Sy.G., sympathetic ganglion. (Gaskell and Bayliss)

The schematic drawing given by Gaskell and Bayliss (Fig. 26*a*) shows the centers of the sympathetic system in the spinal cord, and the relative disposition of the voluntary and involuntary systems. The cells of origin in the lateral horn are indicated at *LH* in Fig. 26*a*.

Antagonistic Innervation of the Vessels.—Although the finding of antagonistic innervation in the visceral territory offers no particular difficulties, the relations that obtain in the case of the vessels of the extremities are somewhat more difficult to interpret. The rami communicantes emanating from the anterior roots appear to contain only the vasoconstrictor fibers. Clinical facts speak for the probability that vasodilator influences travel from the posterior horn through the posterior root, and then by way of the spinal ganglia into the periphery. So we can explain the active hyperemia in the irritated cutaneous territory, when sensory nerves undergo excitation. An irritative reflex erythema¹ takes place, one that is absent when the reflex arc is broken by section of the nerve. The vasodilator impulses appear to have their own fibers, and they leave the spinal cord through the posterior roots, and then course with the sensory fibers through the spinal ganglia to the periphery.

And so it has been accepted by many that the vessels of the trunk and extremities are supplied by an antagonistic double innervation in which constrictor and dilator impulses functionate.

Some time after electrical stimulation of the sciatic stump after section vasodilator changes are noted, while stimulation immediately after section results in vasoconstriction. From this the conclusion has been drawn, that the dilator fibers are preserved longer than those of vasoconstrictor function.

According to Starling, Bayliss and others, besides the main vasomotor center in the medulla there is a series of subsidiary centers in the gray matter of the lateral horns of the cord, giving origin to the fibers that go to make up the white rami communicantes. These centers make possible a certain degree of adaptation between the blood supply of the various parts of the trunk. If the spinal cord of an animal be destroyed, the blood pressure sinks almost to zero, and the circulation comes to an end. The spinal centers, like the chief motor center, are susceptible to changes in the composition of the blood delivered to them. But these centers may gradually take on an automatic function, replacing that of the higher chief center, after the medullary center has been excluded by division of the cord just below the medulla, and after the blood pressure has fallen.

Clinical observations seem to warrant the conclusion that each half of the spinal cord sends vasomotor impulses to both sides of the body. This fact explains the occurrence of such minimal vasomotor deficiency symptoms in the Brown-Séquard lesions.

The Peripheral Course of the Vascular Nerves.—The vasoconstrictor paths are interrupted by ganglia outside of the spinal cord, just as are all the nerves of the vegetative system, and they leave the spinal cord through the anterior roots. We are interested here only with the course of the vasomotor fibers of the extremities, which are similar in their paths to those of the trunk (Fig. 25).

After union of the anterior roots with the nerve bundles emanating from the spinal ganglion, the fibers of the vegetative function of vessel innervation leave the spinal nerve through the ramus communicans albus. In the gangliated cord they make contact with multipolar cells, that give rise to the postganglionic or postcellular nerves. The postganglionic fibers pass through the rami communicantes grisei (gray rami). In their course they accompany the spinal sensory nerve, and particularly the sensory paths. With these they enter the subcutaneous tissues and the vessels of the latter. This

¹ See Chap. XLVI (Dermatographia).

course applies only to the vasomotor paths of the extremities and to the skin of the trunk.

In some of the larger vessels (internal carotid, aorta, and renal arteries) nerve bundles and ganglion cells have been found in the adventitia. Such nerve elements have not as yet been discovered in the vessels of the extremities. In view of these facts, some physiologists have concluded that peripheral vasomotor centers may lie in the immediate vicinity of the vessels, giving these an independent tone. We would then have three different centers, the *cerebral*, the *spinal*, and the *peripheral*. Possibly this third type plays a rôle in the responses due to direct excitation.

According to some investigators nerve fibers are present in the blood vessel walls. Glaser speaks of a reticulum of nerve fibrils in the adventitia, demonstrable with special vital staining methods. In the deeper layers a network is imbedded between the adventitia and media. Between the muscle bundles there are also fine fibrils with nodes. Such have only been found in the larger arteries and veins.

In the case of the smallest vessels fine fibrils can be traced about the external walls, and an intraparietal network also has been recognized.

As for the capillaries they are said to be surrounded by a fine network, there being two accompanying nerves with numerous anastomoses.

According to Sabin, 2 types of nerves are found, forming plexiform nets on and in the walls of the larger vessels. The motor type appears to be distributed so that contact is made with each muscular element. This set of fibers undoubtedly evokes functional vasomotor responses. Dogiel believes that the other type is distributed to the 3 tunic layers of the vessel wall, terminating in flattened end-plates or specialized structure. Such fibers would be of sensory variety.

Müller and Glaser¹ describe fine nerve filaments coursing along the capillaries and encircling these through anastomoses.

Since true ganglion cells of the sympathetic type have not been found in the deeper layers of the vessels, and none at all in the peripheral arteries, the assumption is warranted that vascular response may occur through *direct* action upon the musculature. Indeed, the tonus of this musculature may be preserved after nerve section. Inasmuch as degenerative changes after the exclusion of nerves have not been found in the smooth muscle, Glaser takes exception to the view of those who would postulate a degenerative response in a fashion analogous to that occurring after section of a vasomotor nerve.

Much discussion has arisen as to the course of the reflexes in these territories. Some investigators believe that vascular reflexes originating in the sensory nerves must pass through an arc of which the spinal cord forms a link. The view of Langley, that axon reflexes may account for the responses, is not universally accepted. According to the latter author, an irritation of the skin would pass through the centripetal sensory fibers, only up to that point where the vasomotor paths and sensory diverge, from which the impulse would lead through the vasomotor fibers to the blood vessels. Such would be a peripheral reflex arc without interposed ganglionic cells.²

Some of the more recent authors lean to the supposition that the vasoconstrictor impulses travel by way of the spinal cord; the vasodilator paths, however, may lead to the vessels without passing through the ganglia of the sympathetic gangliated cord.

Dissections made by Potts have demonstrated that, as in the arm, the distribution of vascular nerves in the leg is much more extensive than that laid down in the text-books; further, that the sympathetic supply for the vessels of the lower extremities reaches the main vessels at intervals along their course. Potts also states that the small vessels differ from the large ones, as a rule, in not having special nerve supply, but in obtaining their nerve plexuses direct from the sympathetic plexus on the parent artery.

¹ Müller, *Das Vegetative Nervensystem*, 1920, p. 100.

² See Chap. V and Kroh's substantiation of the theory of Langley, Fig. 27a.

Distribution about the Common Femoral Artery. The branches of the superficial and deep femoral arteries, and the medial and lateral circumflex vessels all derive their nerve supply directly or indirectly from the femoral nerve. The popliteal artery derives its supply in part directly from the N. tibialis, and in addition receives a branch in many cases from the azygos nerve. The same author states that both the main trunk of the vessel as well as larger arterial branches receive supply direct from the nerve trunks and not through the medium of a continuation of nerve plexuses from the parent arterial stem. From these findings it would be difficult to understand the *rationale* of the operation of periarterial sympathectomy (Leriche, Chap. CV), to be described later on.

Summary.—The vasomotor system, therefore, is made up of a structure of superimposed parts, all more or less interdependent. Whilst we note in the nerves supplying the voluntary muscles but two divisions, we must count upon four or more in the vasomotor system. (Some even believe that there may be a vasomotor center in the cerebrum.) Vasomotor paths travel from here with the motor and sensory conducting system through the internal capsule through the subcortical large ganglia. Perhaps in the optic thalamus or in the caudate nucleus, interruption in their continuity takes place through the interposition of new cell groups. From there they are believed to pass further through the pons to the large vasomotor centers of the medulla oblongata. Thence fibers pass through the lateral portion of the spinal cord to various levels in the latter to break up about cell groups in the middle portion of the gray substance, the latter being the spinal vasomotor centers. From these cell groups, fibers again appear that lead to the sympathetic by way of the rami communicantes, and from there pass further into the periphery. At this point in the course, namely, at the gangliated cord or somewhat nearer the periphery, or even in the vessel wall, further interpolation of ganglionic cells may take place. These cells may be regarded as the most distal vasomotor centers. Some authors believe that an additional autonomic function or capacity must be ascribed to the smooth muscle of the vessel musculature.

CHAPTER V

FUNCTIONS OF THE VASOMOTOR NERVOUS MECHANISM

The Vasoconstrictor Nerves.—Experimental data corroborate the view oft expressed that the vasoconstrictor nerves leave the spinal cord by the anterior roots of the spinal nerves from the first dorsal to the third or fourth lumbar inclusive. The white rami communicantes conduct them from the roots to the ganglia of the sympathetic chain situated along the front of the vertebral column, from which point they take varied courses according to their destination.

On leaving the cord (Starling), the vascular nerve fibers carrying vasoconstrictor impulses come to an end in a collection of ganglion cells that either belong to the main chain of the sympathetic or are situated more peripherally belonging to a group of collateral or peripheral ganglia. The fibers leaving the central nervous system are small medullated nerves that end in the ganglion by arborescing around ganglion cells from which a fresh relay of fibers carries the impulses to the muscle fibers of the blood vessels.

The splanchnic nerve is regarded as the most important vasomotor nerve of the body. It receives most of the fibers from the lower seven dorsal and upper two or three lumbar roots, the latter fibers often taking a separate course as the lesser splanchnics. Experimental section of the splanchnic in herbivorous animals, in which the alimentary canal is very much developed, causes a marked fall in general blood pressure.

Vasodilator Nerves.—Whilst at first it was believed that dilatation of arteries is produced only by inhibition of the normal constrictor impulses, another nerve supply antagonistic in function to the vasoconstrictors has been detected in many parts of the body.

Genuine inhibitory nerves to the arterioles are assumed to exist, through which vascular dilatation is produced. This is to be expected and conforms to the rule; for, smooth muscle not subject to voluntary control is usually supplied with two kinds of nerves, excitatory and inhibitory.

Stimulation of the peripheral end of the *chorda tympani* nerve to the submaxillary gland, causes such marked vascular dilatation, that six to eight times the previous amount of blood is made to circulate. Amongst other vasodilator nerves we may mention, the *lingual* nerve to the blood vessels of the tongue, the *small petrosal* to the parotid gland, and the *nervi erigentes* to those of the penis.

It is a mooted question as to whether vasodilator fibers are present in the nerves of the limbs. In experimental stimulation the vasoconstriction produced more than counterbalances any results obtainable through the simultaneous excitation of possible dilator fibers. The dilators apparently do not conduct any tonic influences to the blood vessels, so that the only effect of section of a mixed nerve is that due to the removal of the tonic constrictor impulses, and the vessels in the area of nerve distribution become dilated.

Physiological researches have shown that vasodilator fibers course in the sciatic nerve. The dilator fibers, however, cannot be traced back through the sympathetic system. The observation of Stricker and Morat that dilatation of the vessels of the hind limb can be produced by stimulating the posterior roots of the nerves going to the limb, was confirmed by Bayliss. According to Starling "Stimulation of the posterior roots, either before or after they have passed through the ganglia, causes dilatation of the vessels in the area of the supply of the roots, whatever be the nature of the stimulus employed, whether electrical, chemical, or mechanical. This effect is not destroyed by previous section of the posterior roots on the proximal side of the ganglia, showing that the fibers by means of which the dilatation is produced have the same origin and course as the ordinary sensory nerves to the limbs. Since the vasodilator impulses pass along these nerves in a direction opposite to that taken by the normal sensory impulses, Bayliss has designated them as *antidromic* impulses. So far this phenomenon of a nerve fiber functioning (not merely conducting) in both directions, is almost without analogy in our knowledge of the other nerve functions of the body. There is no doubt, however, that similar antidromic impulses are involved in the production of the so-called trophic changes, such as localized erythema or the formation of vesicles (as in *herpes zoster*), which may occur in the course of distribution of a sensory nerve, and is always found to be associated with changes, inflammatory or otherwise, in the corresponding root ganglia. Moreover evidence has been brought forward that these fibres may take part in ordinary vascular reflexes of the body, that in fact they are normally traversed by impulses in either direction."

In the antidromic vasodilatation, and in the reddening and inflammatory changes consequent upon local excitation, Meyer and Bruce believe that impulses course by way of *axon reflexes*, these being the remains of local reflexes of a primitive peripheral subcutaneous nervous system. All the signs of a local inflammation can be produced by the application of croton oil to the skin or conjunctiva. Nor will destruction of the central nervous system or section of the sensory nerve roots (posterior spinal root or trigeminus) on the central side of the ganglion alter the reactions. If, however, a division peripherally of the ganglion be produced and time be allowed for complete degeneration of the nerve fibers to their peripheral terminations, the application of croton or mustard oil, even to the delicate conjunctiva, is without effect. Similar results follow when the peripheral terminations of the nerves are paralysed by the subcutaneous injection of local anesthetics. Starling says that we must assume that the axons of the peripheral sensory nerves branch, some branches going to the surface, others to the muscle-cells of the cutaneous arterioles.

While Bayliss expounded the theory of antidromic conductivity in the sensory nerve fibers, some of the more recent Continental observers reject this view. According to Bayliss both centripetal sensory impulses course in the sensory fibers to the posterior nerve roots, as well as coincidental centrifugal vasodilator impulses. Continental observers regard this as artificial explanation, all the more so, since existing well-known nerves have

been demonstrated to conduct both centripetal sensory and centripetal vegetative functions. As an example may be mentioned the vagus nerve and the chorda tympani, composed of sensory and parasympathetic nerves. By analogy it could be assumed, therefore, that other nerves in communication with the spinal cord could be similarly constituted.

Recent Views.—Recently the Continental school of investigators have made contributions somewhat at variance with the findings of the English physiologists who were largely responsible for the foregoing facts.

Embryologically the heart forms a part of the total vascular system from whence it would appear probable that both heart and peripheral vessels receive parasympathetic and sympathetic innervation. It is believed that heat regulation depends for the most part upon changes in the transverse section of the blood vessels; that cooling produces an irritation of the parasympathetic and heating a similar response in the sympathetic paths. Up to the present time, however, double vascular innervation has been discovered for but a small portion of the vascular tree.

It is known that the parasympathetic dilator fibers of the chorda tympani pass through the vessels of the salivary glands; and that vasoconstrictor fibers from the cervical sympathetics pass to the same vessels. The double innervation of the vessels of the penis is even more significant. Here vasodilator impulses pass through the N. erigens from the sacral cord (containing parasympathetic fibers of erection), while vasoconstrictor sympathetic fibers (from the lumbar cord) occasion relaxation.

In spite of the warrantable conclusion, concerning a double antagonistic peripheral innervation of the vessels acceptable through analogy and physiological considerations, no definite anatomical corroborative evidence is yet at hand to prove that the vascular nerves of the skin of the trunk and extremities contain parasympathetic fibers. Langley is largely responsible for the view that the points of origin of the thoracic and lumbar vegetative fibers contain only sympathetic fibers. Dresel, Brugsch, Kraus and others express the conviction, however, that this is no longer in accord with modern evidence. Basing their deductions upon the well-known double vegetative innervation of the striated muscles; upon the course of the nerve fibers of the sweat glands; and finally, upon the essential requisite for a parasympathetic vasodilator fiber supply to the vessels of the trunk and extremities:—they believe that such *combinations of sympathetic and parasympathetic cells* of origin must reside in the thoracic and lumbar cord. For such a coincidence is accepted for the dorsal vagus nuclei. Of late, Müller extends the hypothesis of Bayliss, regarding the existence of vasodilator fibers in the posterior roots, into the theory that such paths are constituted of *parasympathetic nerves*. In short, enough data are at hand to allow of the assumption that preganglionic parasympathetic ganglion cells may exist in the thoracic and lumbar cord, from which the striated musculature, sweat glands, and vessels receive additional innervation. Dresel agrees with Müller that we must reject the old view that a dominant vasomotor center exists in the medulla oblongata.

As for the vasomotor reflexes, an arc is thought to exist, one of whose limbs is constituted by centripetal sensory fibers, with a relay station in the cord, through which the impulses then travel through the centrifugal vegetative paths. Such reflexes can be demonstrated after section of the cord, even in the anesthetic territory.

Nerve Influences in Capillary Motility.—Whilst admitting that chemical or humoral factors are capable of influencing the caliber of the capillaries, Krogh has recently rejected his original view that the nervous system does not play an important rôle in capillary activity. In his latest investigation on the submucous capillaries in the tongue of the frog this author has shown

that the capillary dilatation following local trauma is brought about by nerve action. A reflex is established in the sensory nerves; and its course would follow an antidromic direction (axon reflex) directly opposed to that of the sensory impulses (Fig. 27).

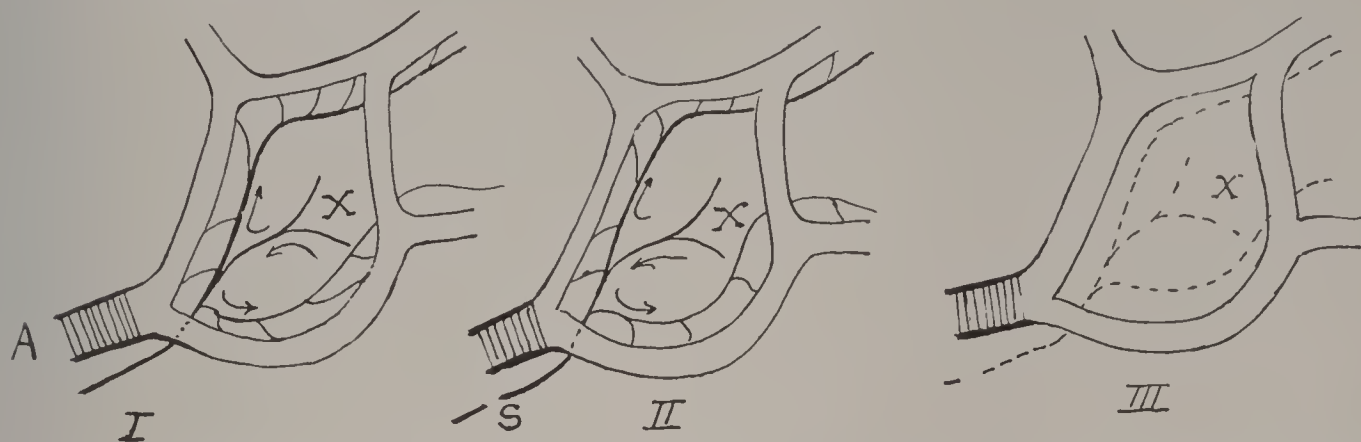


FIG. 27.—Scheme of vasomotor innervation in the responses of capillaries to local mechanical irritants. A, arterioles; S, nerve sectioned. I, A stimulus at X travels over sensory filaments in the direction of the arrow and in antidromic direction back so as to innervate the capillaries; II, shows that the capillary response is maintained even after nerve section; III, shows that the capillary reaction is absent when secondary nerve degeneration has taken place. (Krogh)

These conclusions are based upon the following findings: A puncture trauma brings about capillary dilatation (except when the wall of an arteriole is injured, when contraction is induced). Immediately after section of the motor and sensory nerve of the region under experimentation, no change in the capillary response after puncture follows. Such a result would seem to be independent of the nervous system. But, if the experiment is repeated after degeneration of the nerve has taken place, *the dilating response of the capillaries is absent*. Similarly, local cocainization suppresses the reaction.

Experimental work has shown that section of the spinal cord in animals is followed by an immediate dilatation of all the vessels below the level of the section in the territory supplied by nerves arising below the level of section. Afterwards, however, the vessels contract again, an evidence of functional control in the spinal cord. These facts would tend to corroborate the assumption that the higher centers only motivate the vessel activities. Moreover, destruction even of these portions of the spinal cord is not followed by complete loss of all vasomotor innervation. Although there is temporary vascular paralysis, this gives way to normal vascular constriction after a time. A normal tone of vessels may persist in animals even after the central nervous system has been excluded as a factor in the regulating mechanism. From this it has been deduced that a *peripheral nervous apparatus* or local vascular center must exist. This is represented by the ganglion cells and plexuses that surround the vessels.

Although total loss of the cerebrospinal system is followed by a reduction in the total responsive capacity of the vessels (in animals), nevertheless Lewaschew¹ was able to show that vessels whose vasomotors were paralyzed still gave the well known reaction of contraction and dilatation to changes in temperature. The usual vessel activities or responses to direct mechanical, thermic, chemical and electrical irritation of the periphery are said by Landois to take the circuit of the peripheral vessel ganglia. In such functions the paths would be axon reflexes (Langley²), that is, within sympathetic neurons. True reflexes, however are not confined within the sympathetic system, but usually go through the cerebrospinal paths.

¹ Lewaschew, Virchow's Arch. f. path. Anat., 92, p. 152.

² Langley, Ergebn. d. Physiol., II, 2, p. 818.

Even the veins may contract upon external irritation. Constrict or phenomena are attributed to the venules in some forms of acroasphyxia.¹ Although there is no accord amongst authors regarding the certainty of the presence of vessel centers, it may be accepted as proven that a certain automatism of peripheral action is a characteristic of the sympathetic system.

The Vasodilator Function.—The action of the vasodilators is demonstrable when, after section of a nerve, irritation of its peripheral end is followed by dilatation of the innervated vessel, whilst the mere interruption of continuity produces no constriction of the lumen. The vasodilators do not appear to have influence upon the normal tone. Up to the present time no center has been found for these, although one is said to exist in the medulla oblongata. The course of the vasodilator nerves is still uncertain. In some organs they course as special nerves; in other parts of the body they are mixed with the vasoconstrictors. According to Stricker and Gärtner² the plexus sacralis contains vasodilator nerves for the lower extremities.

In the case of the vasodilators, also, subordinate centers are assumed to reside in the spinal column. Just how the vasodilators work, has not been discovered. Some believe that their action is direct upon certain longitudinal muscles in the vessels. The view that they act in an inhibiting fashion on the peripheral ganglia is more acceptable. Others (Lewandowsky) assume that the vasodilators act directly upon the circular muscles of the vessels without intervention of peripheral ganglia, making these yield their tone.

Excitation of the vasodilator center may be brought about directly or reflexly. When venous blood or a poison, such as chloral hydrate is given in small doses, a direct effect is produced; or, reflexly, as in erection, through sensory stimuli. Even the body temperature may be influenced through irritation of these centers.

Antagonistic Innervation of the Vessels.—According to Müller³ it is believed that the regulation of the size of the vessel lumina is also under the control of two separate systems of antagonistic action, namely, from the gangliated cord of the sympathetic and from the parasympathetic autonomic system. Such is the case in the other visceromotor functions.

The relations that obtain in innervation of the vessels of the trunk and extremities are somewhat difficult of interpretation. The rami communicantes from the anterior roots appear to contain only vasoconstrictor fibers. Clinical facts point to the possibility of the transmission of vasodilator influences from the posterior horns through the posterior roots, whence they attain the periphery through the spinal ganglia. Strong irritation of sensory nerves leads to active hyperemia in the irritated territory. This is a reflex phenomenon, for after section of the nerve with interruption of the reflex arc, the hyperemia is absent.

Whether the vasodilators are also in communication with ganglia of the gangliated cord, is doubtful. Bayliss was able to produce vascular dilatation in the lower extremity after irritation of the posterior roots, even when the abdominal sympathetic was removed.

Not only is it accepted to-day that there are antagonistic double innervating paths for constrictor and dilator impulses, but it would seem that the conductivity of the dilator fibers persists longer than that of the constrictor paths (Müller).

Still it is not necessary to assume that two separate centers must be present in the brain for vasodilatation and vasoconstriction. Indeed,

¹ Briscoe, see Chap. VII.

² Stricker & Gärtner, Wien. klin. Wchnschr., 1889, p. 980.

³ Müller, Das Vegetative Nervensystem, 1920.

the sudden blush of the face could hypothetically be brought about through paralysis of the vasoconstrictor center. It is more plausible that from a single vasomotor center influences emanate that simultaneously are of an inhibiting nature, and others of an exciting or vasoconstricting quality.

Physiology of the Large Vasomotor Centers.—Physiologists believe that the vasomotor centers are ordinarily in a state of mid-tonic excitation. From them impulses are constantly flowing that induce a middle grade of contraction of the vessel musculature, thereby producing the normal vascular tone. Fluctuations in the state of activity of the centers run parallel with the respiratory movements. According to Simon the function of internal secretions expresses itself in the production of hyper- or hypotension. These effects are in a state of equilibrium under physiological conditions.

The vasomotor centers may be directly or reflexly stimulated. Direct excitation results from the action of the gas content of the blood circulating in the medulla oblongata. A marked venous admixture causes correspondingly strong stimulation of the center leading to contraction of the arteries.

Irritation of certain centripetal nerves can produce contrary reflex effects either exciting or depressing the centers (pressor and depressor nerve fibers). Some authors believe such fibers are present in all sensory nerves. According to Lovén irritation of sensory nerves causes firstly pressor effects; but continued and intensive stimuli lead to depressor effects and vascular dilatation. Weak electrical or tactile stimulation of the skin, or thermic influences call forth depressor effects.

According to certain authors, pressor effects can be obtained in a reflex way through the action of weak electrical irritation or through the application of cold or warmth to the skin. Hallion and Comte¹ produced vasoconstriction in a reflex way through various sensory irritants. Experimental investigation has shown that most of the irritants produced vascular constriction. Some authors have tried to show that sensory regulating fibers are present in the vessels themselves.

The nerve control of the vessels differs somewhat from that of other organs whose activities are influenced by the vegetative nervous system. In the organs, peripherally situated ganglionic cells (such as the Auerbach plexus) take up impulses that modify the activity of the organs themselves. They are regarded as peripheral reflex or automatic centers, and have been compared to differentiated anterior horn cells. As such, motivating and inhibiting extracentrally situated sympathetic and parasympathetic nerves constitute the path for nerve control. But these reflex and automatic centers of ganglionic nature appear to be absent wherever the function is an uncomplicated one as in the case of the vessels.

Edinger believes that sensory impressions are produced on sympathetic cells lying directly in the vessels; and from these cells reflex contractions may take place in the arterial wall through other fibers.

It is well known that section of the cervical region of the sympathetic brings about reddening and warmth of the ear of the corresponding side in experimental animals. The vessels dilate and the blood stream in the affected part is retarded. The blood pressure is increased, the arteries pulsating actively, the pulse even being noticeable in the veins. Irritation of a peripheral vasomotor nerve itself brings about pallor of the corresponding part, coolness, reduction of temperature, and constriction of the vessel. In the case of smaller arteries such constriction can be so marked as to completely

¹ Hallion & Comte, *Arch. f. Physiol.*, 1894, p. 381; 1895, p. 90.

occlude the lumen. Continued excitation, however, finally brings about exhaustion of the nerve with the manifestations of paralysis.¹ *These observations are of exceedingly great clinical interest in that they give us a clue as to the pathogenesis of many of the vasomotor affections, such as erythromelalgia, Raynaud's disease and the cases of vasomotor instability.*

It is an important observation that the effect of irritation or paralysis of vasomotor nerves varies considerably in intensity in different vascular territories. For instance, the vessels of the ears, nose, fingers and toes are most easily influenced, other regions being less intensively acted upon. These varying effects may depend to a certain extent upon the architecture of the arteries.

The Vasomotor Tonus.—It is not necessary to assume that there are circumscribed areas controlling vegetative innervation of vasomotor function. The dominating vasomotor center in the brain appears to functionate in conserving and regulating the general vascular tonus. Various emotional states are believed to cause qualitative alterations in the cranial vasomotor centers, from whence fluctuations in tonus are produced through activation of vasomotor centers in the cord. We do not know whether the tonic influences from the mid-brain are necessarily intimately connected with nerve fibers, or whether they are conducted through the gray substance, or through the substantia gelatinosa. For, as in electricity, special conducting paths are not essential. Müller designates the status of the general nerve excitability as a biotonus which may suffer alterations under various conditions. Particularly in the spinal cord are such changes possible, as manifested by increased intensity of reflexes during emotional states. This tonus may also be susceptible to sensory impulses. And, *therefore, the theory has been proposed that pain impulses, or other tactile sensory impulses, may cause a generalized change in excitability of the gray substance of the spinal cord.* Such modification in the *tonus* of the spinal cord would in turn react on the function of the spinal vegetative centers, such as the vasomotor cell group. This theory is supported by the belief that it is quite impossible for all sensory paths to be in immediate connection with all vegetative centers in the spinal cord, medulla oblongata and mid-brain. Clinically, noteworthy is the great vasolability manifested in the lower extremities of thrombo-angiitis obliterans and to a less degree in the extremities affected by atherosclerotic and other arterial disease. In the former malady it not infrequently follows persistent pain. It is more than likely, that just such a *tonus alteration* in the spinal cord, in consonance with the above hypothesis, may obtain in thrombo-angiitis obliterans, and account for the vasomotor lability of many of the cases.

The tonus that dominates the spinal vasomotor centers appears to be reestablished in the distal portions of the spinal cord shortly after experimental section of the spinal cord. It fluctuates according to the sensory impressions that arise in the detached portion of the spinal cord. After total section, irritation of the sciatic nerve produces increase in blood pressure. When the feet in a paraplegic are exposed to cold impulses, the subsequent vasoconstricting effect is limited to the lower part of the body. This observation seems to speak for the view that the dominating tonus in the spinal vasomotor centers is conducted not through long isolated paths, but rather controls the whole of the gray substance and varies or is changed through numerous sensory influences. Of these latter, pain and temperature are the most important. Such impulses do not necessarily come to our consciousness, nor reach the cranial vasomotor centers, as is exemplified by the paraplegic. It would appear that the alteration in tonus occupies the total transverse area of the cord, since on the action of cold, not only vasoconstriction but simultaneous pilo-erectations, contraction of the scrotum and the skin of the penis, as well as contractions of the striated

¹ Compare with explanations of erythromelia in Chap. XLI.

muscles are observed. It is also noteworthy that heat elicits dilatation of the vessels, sweat and relaxation of the scrotum.

Histologically the cells resemble the ganglion cells in the sinus nodes and in the auricular septum of the heart. The small ganglion cell group and the single cells that are sometimes found in small nerve bundles are found in loose connective tissue of the adventitia. Although such cells have been found in the vessels leading to the viscera cells and in the aorta, they have not been demonstrated thus far in the vessels of the extremities.

It is not unlikely that in the neighborhood of the vessels, or in the vessel walls, peripheral vasomotor centers capable of an automatic tonic function exist. These have been called vasomotor centers of the third class in contradistinction to the first (cerebral) and second (spinal) category. It is believed that the vessel activities resulting from direct irritation take place through the intervention of these centers. Indeed, by means of special tinctorial methods, nerve elements have been demonstrated in the vessel walls.

According to Glaser¹ it is possible to demonstrate a network of fibers in the adventitia of the veins if we employ vital stains and young subjects. A further network of nerves is seen between adventitia and media; also between the muscle bundles of the media, a branching network of finest fibrils with knobbed nerve filaments has been found. Some of these travel the whole media and penetrate into the intima. These appearances have been demonstrated for all of the larger arteries and veins. Even the capillaries are enmeshed with nerve filaments that show numerous anastomoses.

In the deeper layers of the vessels ganglionic cells have not been found. Inasmuch as ganglionic cells have not as yet been demonstrated in the peripheral arteries, we cannot exclude the possibility of direct muscular vessel reactions to mechanical or thermic stimuli.

As for the distal constrictors and vasodilators very little is known. Indeed, the old concept that the vasoconstrictors lead to the annular musculature and the vasodilators to the longitudinal muscle fibers has not been conclusively proven, all the more so, since the smallest vessels contain no distinct longitudinal muscle bundles.

Recent Views on Physiology.²—The peripheral parasympathetic and sympathetic fibers have an antagonistic influence upon the single vegetative organs. Dresel believes that alterations in the functional condition of the cells (muscle or glandular cells) may be brought about through nerve impulses coursing through this system; and that the *modus operandi* is one in which the surface tension or potential undergoes a change. Such deviations may be produced in the electrolytic equilibrium of calcium and potassium, with the balance in favor of one or the other Ion. This with other biochemical alterations would effect functional derangements in the cells (such as muscle and gland cells).

A coordination of the antagonistic effects of the parasympathetic and sympathetic nerve impulses is realized through the central vegetative nerve stations. The view until recently widely accepted, to wit, that irritation of one system induces a diminution of tonus in the other system (Eppinger and Hess), seems to be controverted by recent investigations. Thus it has been shown (Dresel) that every parasympathetic excitation is followed by one of the sympathetic and conversely. The mechanism responsible therefor is one that tends to conserve the dominant equilibrium. This is accomplished through a regulating mechanism in the subthalamie center, which responds to every change of temperature, of blood pressure, or of blood sugar content, by influencing the subordinate parasympathetic and sympa-

¹ Müller, *loc. cit.*

² Personal communication from Kurt Dresel of Berlin.

thetic cell origins. For example, if the blood pressure increases by virtue of irritation of the sympathetic (adrenalin) a parallel stimulation of the parasympathetic paths follows through this regulating mechanism, with the purpose of limiting an inordinate increase of pressure and of restricting it to a certain threshold. These phenomena may be compared with the well-known manifestation of *successive induction* (Sherrington) occurring in the animal nervous system. According to this view, coincidently with every reflex, agonistic as well as antagonistic impulses are evoked to check excessive motion.

The above-described regulation may be motivated through the direct action of chemical and physical blood changes upon the subthalamie centers (of temperature, sugar content, Ion content, blood pressure, etc.). The subthalamie center takes a subordinate position to that in the corpus striatum, for the latter is in control of the vegetative function. Indeed, it is believed that the impulses emanating therefrom determine the threshold. This threshold (for temperature, blood sugar, Ion concentration and blood sugar) may be attuned to different levels, through alterations in excitability and state of excitation of the striate body.

Dresel compares the activity of the vegetative centers with a thermostat in which the above functions may be symbolized. The mechanism for regulating heat can be set for varying degrees such as 42° C., 37° C., or 26° C., through the action of the center in the corpus striatum. Just as the regulatory mechanism of a thermostat reacts to changes of external temperature, so also do the subthalamie centers, whose function it is to conserve an equal temperature; and this is effected in that the subordinate centers (points of origin of the parasympathetic and sympathetic in the mid-brain, medulla and cord) are made to respond accordingly. Similarly for all other vegetative functions there is a very accurately and delicately attuned mechanism for the conservation of proper equilibria. It is then easily understood how very slight alterations may bring about very severe symptoms.

The Vascular Nerve Centers.—It has already been previously mentioned that the cellular points of origin for the peripheral vegetative vascular nerves are to be found in the medulla and in the spinal cord, where they receive their impulses from the superior vascular centers in the subthalamie regions and corpus striatum. Karplus and Kreidl had already demonstrated the existence of nerve communications between the subthalamie region and cord (since irritation of the mid-brain failed to produce typical effects on the vessels after section of the cervical cord). Dresel obtained anatomical proof in the finding of retrograde degeneration in the cells of the subthalamie region after section through various levels of the spinal cord. Furthermore, this author showed that certain ganglionic cells in the subthalamus undergo variation in excitory state, through fluctuations of blood pressure.

It is well known that clamping or ligation of the carotid leads to increased blood pressure in the arteries (with the brain excepted). Such hypertonia results through regulatory impulses emanating upon the mid-brain. That such must be the case was proven by the absence of such an eventuality after section through the corpora quadrigemina. So it has been assumed that the regulatory impulses leading to increased blood pressure are evoked through the diminished blood supply in the brain, and have their source in the mid-brain.

Analogous phenomena are to be found in the so-called "vagus pulse." This follows injection of adrenalin, and has been said to be due to direct action of adrenalin or increased blood pressure upon the vagus center. Perhaps, however, this vagus effect is nothing but a manifestation of regulatory impulses from the mid-brain, in response to the increased blood pressure. This conclusion is warranted on the basis of the observation, that the vagus pulse can be prevented by preliminary separation of the medulla and corpora quadrigemina through section (whence adrenalin injection will be ineffective in spite of the continuity of the peripheral nervous system). Although Karplus and Kreidl had already noted the vasoconstrictor effect that follows direct electrical irritation of the hypothalamus, no functional conclusions were drawn by these authors concerning blood pressure phenomena in general.

The corpus striatum is said to have a distinct influence upon the vascular nerves and upon blood pressure (Dresel).

If a point in the nucleus lentiformis (globus pallidus) is accurately stimulated with a double electrode, the introduction of faradic current brings about considerable fall in blood pressure, which continues for a time after cessation of the electric irritation and then gradually disappears.

Here we see then that there is a distinct relationship between blood pressure level and the excitatory condition of the corpus striatum (just as is the case with the thresholds of other blood components).[†]

The psychic and sensory influences upon the whole vegetative nervous centers probably take place by way of the center in subthalamie and striated centers. Here, then, there is disparity between animal and vegetative nerve functions. *In the former, actual areas of projection in the cortex of the brain exist, while the absence of such for the vegetative system would seem to have been confirmed by researches.* For, dogs without cerebral cortex may be wholly devoid of any vasomotor disturbance.

In the vegetative system, changes of vascular girth run parallel with changes in total metabolism. With such vascular alterations there is usually a generalized reversal, inversion or modification in the vegetative system.

Then again the question has been ventilated as to whether delimited vascular territories are represented in the circumscribed vegetative centers. Indeed, experimental and clinical experiences would seem to point to the possibility that certain ganglionic cells do control the regulation of certain vascular territories. It has been even suggested that excitatory changes in the centers of the striatum and hypothalamus may be induced so as to bring about limited vascular alteration in an extremity. Emotional impulses are said to evoke such phenomena. Since cortical centers are absent, the separation of vascular territories in central stations must needs take place at a higher level than at the points of origin of the peripheral vasomotor nerves (medulla and cord).

Viscero-vasomotor Reflexes or Vaso-vasomotor Reflexes.—Clinical observations have suggested that not only do viscero-sensory reflexes exist as exemplified by the Head zones, and visceromotor reflexes as in the so-called “*défense musculaire*,” but that there may be viscero-vasomotor responses or even vasomotor responses secondary to irritations of vascular origin. Zak¹ describes hyperemic or erythematous zones below the fossa jugularis, and just under the mesial half of the clavicle in cases of aortic disease. These areas are roughly of semilunar shape, and the skin in this region responds with abnormal activity to mechanical irritation. In some cases the vasomotor centers are hyperirritable through impulses sent from the diseased aorta; in others, the centers themselves are primarily in a state of increased irritability.

Other visceral affections such as pulmonary diseases may give similar vasomotor zones. Zak states that in about one-third of the cases of aortic disease distinctly demonstrable semi-lunar erythematous manifestations are present; and that these are evidences of local vasomotor hyperexcitability with corresponding segmental alterations in the spinal centers. There is a certain degree of parallelism between the vasomotor and sensory hyperexcitability.

Müller² describes a clinical method based in all probability upon reflexes through the spinal segment corresponding to that irritated. A ring is pressed against the skin, and the included cutaneous area rubbed energetically with the end of a match-stick, so as to produce a somewhat painful sensation for a period of 10 seconds. Thirty to 60 seconds later and after the cessation of the painful irritation there will arise in addition to the hyperemia within the boundary of the ring, a second hyperemic zone extending for a considerable distance beyond, the direction of this rubor being in accordance with the cutaneous segments, that is, more or less vertically over the arm, horizontally over the trunk.

¹ Zak, Wien. klin. Wchnschr., 25, 1920, also Wien. Arch. f. klin. Med., IV, p. 209, 1922.

² Müller, Ztschr. f. Nervenhe., 47, 48, 1913.

Goldscheider,¹ in some clinical experiments applied a clamp to pinch the skin for 1 or 1½ minutes. Besides the manifestation of pain and a cutaneous areola of rubor, an additional girdle-like hyperalgesic zone appeared over the trunk, or a longitudinal vertical streak over the extremities. Similarly a hyperemic zone developed presumably through reflexes passing by way of the spinal segments.

Therefore, just as a cutaneous zone of hyperalgesia corresponds to a state of irritability of the sensory fibers and ganglionic cells of the corresponding segments, so also, it is now believed that an increased excitability of the vasodilator centers may take place. Therefore, in addition to so-called viscerosensory reflexes and visceromotor reflexes, a viscerovasomotor reflex may occur (*Mackenzie*).

These observations give further foundation in analogy to the warrantable assumption that through disease of the arteries, as in thrombo-angiitis obliterans, and partly by reason of the pain impulses often or continuously traveling in such cases, vasomotor reflexes establish themselves, and are responsible for the increased vasolability (vasomotor neurosis) observed in such cases; and perhaps also for the rubor under certain conditions.²

Pain and the Sympathetic.—The exact rôle of the sympathetic system in the production of pain is not known. There seems to be no doubt but that centripetal impulses occur in the sympathetic system, and further, that stimulation of these fibers may occasion pain. The origin of a pain of sympathetic causation probably depends upon the quality of the irritant. Numerous theories have been advanced to explain vascular pain. We know that pressure upon arteries produces painful impulses. Stimulation of the centripetal nerve fibers of the blood vessels, even though unproductive of pain sensation under ordinary circumstances, may produce such in exceptional conditions. Dogiel asserts that the perivascular tissue usually contains medullated nerve fibers, and Vater-Pacini bodies occur in the adventitia. Cassirer believes that direct irritation of the vessel wall through its sensory elements accounts for the pain in erythromelalgia; for, the vasomotor and sensory irritative symptoms roughly correspond in their distribution. In the *acroparaesthesiae* irritative conditions of the vasosensory fibers may also be responsible for the symptoms.

Summary of the Vasomotor Mechanism.—A reference to Fig. 27 will tend to clarify the concept of the mechanism of vasomotility. Through the four neurones, (*a*) cerebrobulbar, (*b*) bulbospinal, (*c*) spinosympathetic, and (*d*) sympathicomuscular, the brain and the three relays are brought into communication with each other and with the periphery. Since vasodilator fibers have only been found in certain special regions, they are not represented in this schematic drawing. Generally speaking, we regard loss of vascular tone as due to vasoconstrictor paralysis, and vasoconstriction as the result of vasomotor stimulation.

It is comprehensible then, that a lesion of the ventral horn is followed by vasomotor paralysis if a discontinuity between the third set of neurones (*c* in Fig. 27*a*) and the central cell group is effected. So also, breaks in the connections of the bulbar and spinal centers (*b*) through lesions of the lateral columns may have the same result.

According to Bing,³ spinal vasomotor paralysis, whether produced by destruction of the vasomotor centres in the ventral horn, or by interruption of the vasomotor fibers in the lateral columns, seldom reveals itself, and then only in its earliest stages by redness and heat of the skin. The skin in the territory innervated by the affected regions of the cord, becomes cold and cyanotic, a condition that may ensue forthwith after the occurrence of the lesion, or may replace a transitory hyperemia.

A glance at the vasomotor paths will demonstrate at once that central lesions interrupting paths in the spinal cord would have an action over extensive circulatory territory. The local manifestations of vasomotor derangement seen in the diseases described here, are limited to such an extent as to warrant the supposition that either more peripheral disorders of innervation are responsible, or isolated ganglion or horn cells only partake in the neurotic

¹ Goldscheider, Ztschr. f. klin. Med., 85, 1918.

² See Chapters XLVI and L (Erythromelia and Pain in Thrombo-angiitis).

³ Bing, R., Regional Diagnosis in Affections of the Brain and Spinal Cord, Transl. Rebman, New York, 1913.

disturbances. A more detailed discussion will be found under the chapter on the "Vasomotor and Trophic Neuroses."

In forming a correct concept of the vegetative functions we should not confine their paths to the gangliated cord, but include as important elements the higher centers in the spinal cord and brain. Although exact localization of lesions that could evoke certain vasomotor neuroses is as yet not feasible, enough data are at hand to make us suspect that the intermedio-lateral region

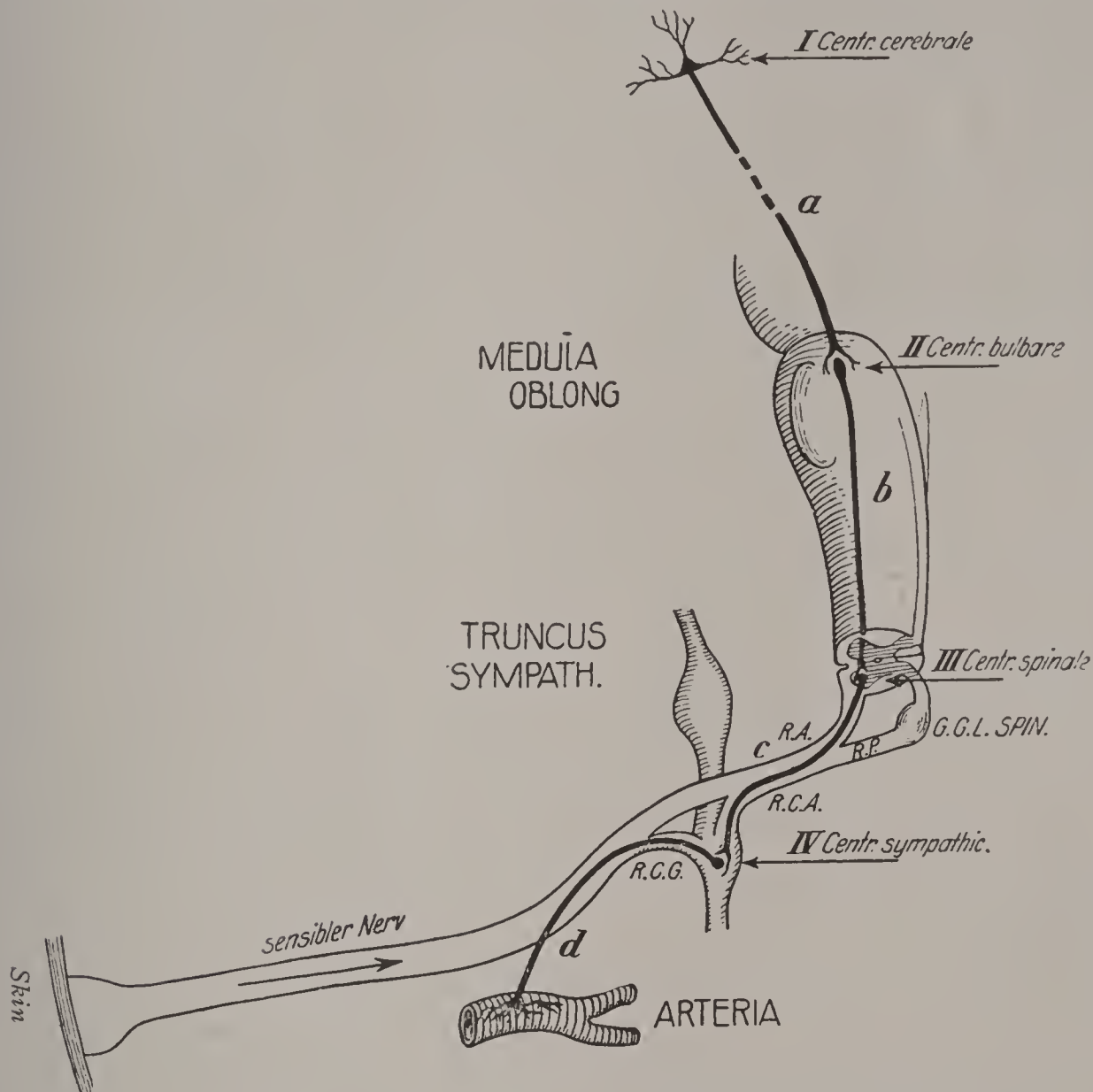


FIG. 27a.—Scheme of vasomotor mechanism. (Bing)

of the posterior gray substance may be the seat of some of the causal lesions in certain of the vasomotor and trophic disorders. But derangements in the reflex arcs, too, can be regarded as etiologic factors.

Cassirer expresses the view that a disturbance in the reflex mechanism between sensory and vasomotor systems could account for many of the cases of vasomotor and trophic neuroses and their trophic lesions of the skin.

Various hypotheses have been offered as to the course of the reflex arc, alterations in which may lead to vasomotor and trophic manifestations. Vasosensory fibers may exist and make a portion of the afferent elements of the sympathetic. Excitation of these is believed to account for the extent and quality of the peculiar pains of which cases of vasomotor and trophic neurosis complain. So, too, in thrombo-angiitis obliterans it is not unlikely that some of the varied forms of pain, particularly those associated with a state of marked vasomotor instability may owe their origin to the excitation of vasosensory nerves (Chap. L).

In further support of the reflex theory of vasomotor innervation, is the circumstance that irritation of sensory nerves has a greater influence on vasomotor tone (especially vasodilatation) than mere section of the sympathetic. The reflexes need, however, not be confined to the sympathetic system, a territory within which such phenomena do not seem to take place, but may take place through the intervention of additional spinal sensory paths.

CHAPTER VI

PHYSIOLOGY OF THE PERIPHERAL CIRCULATION

Elementary Principles.—It may not be amiss to summarize some of those fundamental facts concerning the general circulation that have a direct bearing on the blood flow in the extremities.

Although the laws governing a constant flow of fluids through rigid tubes apply to those with elastic walls (as arteries and veins), a distinct difference exists when fluid is forced into these intermittently and rhythmically. Fluid thus driven into rigid tubes is evacuated interruptedly; in elastic tubes, however, an intermittent pulsatile stream may be converted into a continuous one. The distended elastic walls of the tube exerts such pressure on the contents when the inflow ceases, that the current becomes continuous even during the pause in the main propelling force.

With the heart as the pump, the elastic arterial walls act in this way, and, during the diastole the current in the capillaries is continuous. The arterial elasticity, therefore, is of considerable moment in its influence on the cardiac work. In view of the participation of the arterial walls in the propulsive mechanism, the total cardiac work is under normal circumstances commensurately lessened.

The circulation of the blood conforms, then, to these principles and is modified by the vasomotor innervating mechanism.

Let us briefly discuss here some of the hydraulic principles that govern the blood flow, in so far as they may clarify our concepts of the circulatory affections of the extremities; the nerve control and its influences shall be given consideration elsewhere.

The volumetric increase of the arterial tree is proportionate up to a certain limit to the internal pressure, only to diminish over this point. Furthermore, the more peripheral the arteries the greater the dilatation with equal increase in blood pressure. As the arteries become less elastic with age and disease, the nearer does their function approach the qualities of the rigid tubes.

The pressure in, and the volume of blood delivered by the arteries are dependent on a number of factors; namely, (1) the supply to the heart; (2) the frequency and force of the heart beat; (3) the resistance in the arteries; (4) the viscosity of the blood; (5) the quantity of blood; (6) the changes in the flow under special circumstances; and (7), the changes in cardiac work.

1. It is clear that the quantity of blood delivered by the cardiac pump must be related to that quantity which is emptied into the heart through the large veins. Many experiments have demonstrated that with other conditions unaltered the volume of blood delivered per minute increases in proportion to that supplied to the heart.

2. If a sufficient quantity of blood enters the heart through the veins to fill it during diastole, the volume of blood delivered by the heart per minute is directly proportionate to the frequency of the heart beat. This is true up to a certain limit only; for as the diastole becomes shorter its duration may be insufficient to permit of adequate filling of the heart. And so from this point on the amount of blood that is ejected during the systole becomes smaller and smaller until finally the volume per minute is less than that which the heart would deliver during periods of diminished activity. Whilst these facts are based on physical laws, under ordinary circumstances it is maintained that the volume of blood delivered per minute, as well as the pressure, does not vary with the frequency of the heart beat within certain limits, when ever the resistance to the vessels remains unchanged.

3. Increased resistance offered by the arteries may cause a rise in blood pressure. Contraction of the vessels in a large territory (or ligation of a large vessel as the abdominal aorta) increases the pressure. With moderate increase of the resistance the heart may either deliver an equal amount of blood during a unit of time, or a greater amount. In the latter case, rise of pressure follows. Should a marked increase of resistance take place, the quantity of blood delivered becomes smaller and finally stasis of blood in the heart may result. Nature has provided a reflex mechanism, which, under certain circumstances, brings about dilatation of the arteries with commensurate relief to the heart (through the depressor¹ nerve, irritation of whose central end brings about fall of blood pressure). The autonomic action of the capillaries² is now recognized as capable of playing a distinctive rôle. Krogh showed that most of the blood capillaries in a muscle when at rest are to be found in a state of contraction, their lumina not being too small for the passage of red blood corpuscles. This functional exclusion of the capillaries goes hand in hand with a reduction in the activity of the muscle fibers and with the diminution in the need of oxygen, glucose, etc. As soon as the circulatory demand becomes more active by virtue of enhanced muscular function, the caliber of the capillaries becomes greater, they dilate, and the flow of blood in the muscles becomes accelerated. In reality the contracted capillaries are never completely closed, but allow the blood plasma to circulate.

Besides this functional response on the part of the capillaries, alternate dilatations and contractions in certain of their territories may occur spontaneously from time to time by reason of chemical influences.

4. Changes in the *viscosity* of the blood are said to alter the resistance offered to the circulation independently of alterations in the vascular patency. It has been shown that the internal friction of the blood in certain animals is $3\frac{1}{2}$ times as great as that of distilled water. The non-defibrinated blood of animals and of the human is believed to possess an internal friction of 4 to 5 times that of distilled water. After blood letting this friction diminishes; after feeding animals it increases. The viscosity of the blood also has been reported as being increased by multiplication of the red blood cells, and reduced by administration of salt solution. With diminished viscosity, the heart may, in a unit of time deliver larger quantities of blood than normal without appreciable increase in the blood pressure. Perhaps this phenomenon explains the apparent improvement in the general condition and in the circulation of some cases of thrombo-angiitis obliterans after the administration of large quantities of Ringer's solution subcutaneously or through the duodenal tube (Chap. LXV).

5. The total quantity of blood is of no mean importance in determining the volume of blood delivered into the vessels. Increase of blood pressure may be obtained by inhibition of fluid through the intestinal tract, under the skin, and by transfusion, with consequent delivery of larger quantities of blood into the vessels.

6. Exercises and physical work increase the frequency of the heart beat with consequent increased demands upon the circulation in the arteries. Increased blood pressure may follow and the volume of blood delivered per minute may increase from 3 to 7 times the normal. Other external influences (such as obtain with baths), influence the circulation. The hydrostatic pressure bath is known to exert a distinct effect on the circulation.

7. The response on the part of the heart muscle to changes in the circulation must also be taken into consideration in an estimation of the quantity of the blood delivered. And so it is not always the greatest arterial pressure that evokes a corresponding cardiac activity, but moderate demands or moderate increases of pressure.

Measure of Blood Flow in Extremities.—Perhaps we could obtain a better appraisal of the adequacy of circulation in the peripheral part of a limb by a knowledge of the so-called mass movement of blood. It is conceded that arterial pressure is not in itself an index of the measure of the flow.

¹ This nerve crosses into the cardiac plexus, arises in two routes, one from the vagus, the other from the inferior laryngeal.

² See Chap. on Physiology of the Capillaries.

Stewart¹ has suggested an ingenious method of measuring the blood flow, which he regards as simple and accurate enough for clinical purposes. The method is based upon the fact that the amount of heat produced by a part, like the hand during rest, is negligible in comparison with the heat conveyed to it by the arterial blood. Determination of the amount of heat given off to a calorimeter in a given time in its relation to the temperature of the arterial and the venous blood, permits of calculation as to how much blood must have passed through the part.

Perhaps the wider adoption of methods such as these will prove of some value in the circulatory affections of the extremities.

Some of the results obtained by the calorimetric measurement of blood flow through the extremities may be thus summarized (Stewart).

In arteriosclerosis the blood flow in the hands is smaller, and the contralateral vasomotor reflexes are less pronounced than normal.

In cases where there were inequalities in the blood flow of two hands (through mechanical causes, ligation, embolism, compression) the stability of the ratio of the flow in successive measurements was found characteristic. Tests made at long intervals demonstrated the development of collateral circulation by changes in the ratio of the blood flow in the normal and affected parts. A feature diagnostic of the organic impairment of the circulation was found to be the impossibility of abolishing or greatly altering the flow by the artificial production of vasomotor changes (through external temperature). In other words, temporary vasomotor instability could be made to give different readings in an artificial way.

Inequalities of blood flow in two hands or feet of the nature varying in degree from day to day, and such as could be abolished, produced, increased or reversed, by changing the external conditions, were interpreted as due to unequal activity of the vasomotor mechanism on the two sides.

In 3 cases of Raynaud's disease the hand flow was subnormal; in the more advanced cases very much below the normal.

Stewart summarizes the application of his method as follows:

"The arterial pressure is not in itself a measure of the flow. With a high pressure the flow may be small, with a relatively low arterial pressure it may be large. Indeed, in cases of marked arterial hypertension the blood flow in the extremities has been found subnormal, the high blood pressure being associated with constriction of peripheral vessels and under-irrigation of peripheral parts. If the brachial or femoral artery were obstructed by a clot (or a ligature) the pressure in the artery central to the block would be at least normal. But this would be of no consequence to the patient and would not give the physician any information in regard to the important question, how much blood was passing through the endangered part below the block. The same is true of more limited lesions involving one or both hands or feet, or portions of them. In a considerable group of pathological conditions in which the blood vessels of one or more extremities are involved either primarily or secondarily (thrombo-angiitis obliterans, Raynaud's disease, thrombosis associated with the puerperal state, embolism, etc.) measurements of the blood flow from time to time may yield information of importance, not otherwise obtainable.

In this way the physician may learn: (a) Whether the blood flow is so small that gangrene is probably imminent, although it may not yet have declared itself. A blood flow around the critical level would, of course, emphasize the importance of sedulously protecting the part against mechanical injury or cooling. (b) Whether the vascular condition is stationary, improving or growing worse. (c) The effect, if any, of therapeutic measures (vasodilator drugs, baths, Bier's bandage). In certain cases the diagnosis between a functional vasomotor affection and a mechanical block, due to embolism, thrombosis or anatomical narrowing of the vascular lumen, can be made by testing the effects of vasodilator drugs or changes of external temperature upon the blood flow. A mechanical block will obviously resist such measures, and the blood flow will remain small, while a

¹ Stewart, Harvey Lectures, 1912, p. 86 (Lippincott).

functional (vasomotor) block may open up. In cases where it is proposed to tie an artery, information as to the probable adequacy of the collateral circulation immediately after ligation could sometimes be obtained with advantage before the operation by blood flow measurements with the artery compressed and open (Matas). In several cases in which the innominate and right carotid were tied for subclavian aneurism (Hamann) comparison of the flow in the two hands enabled the gradual establishment of the collateral circulation to be followed till it was adequate for the normal functioning of the right arm. In cases of injury to the nerves of a limb, especially unilateral injury, information of value in the diagnosis can sometimes be obtained by blood flow measurements, paralysis of the vasomotors in the injured nerve trunks leading to definite changes. In early brachial neuritis, *e.g.*, the flow in the corresponding hand is likely to be increased. Such measurements have aided in discriminating between pressure on the subclavian artery and injury to the brachial plexus as the cause of certain symptoms in the arm and hand."

"In the study of pathological conditions of the circulation in the extremities it is sometimes useful not only to determine the rate of the blood flow, but also the degree in which it is affected reflexly through the vasomotor system. It is perhaps not too much to say that the proper application of reflex tests is as important in the investigation of diseased conditions of the vasomotor system as in the investigation of diseased conditions affecting the skeletal affections of the extremities. For, one of the most characteristic properties of the cutaneous circulation (and the circulation of the hands and feet is essentially cutaneous), is the variation in its rate according to the intensity of the metabolism and the temperature of the environment. And this adjustment is brought about largely through vasomotor reflexes.

The intensity of the vasomotor reflexes elicited by heat and cold can be estimated by immersing one hand or foot in cold or warm water, while the blood flow in the other is being measured. (A reflex vasoconstriction is associated with a diminished flow, a reflex vasodilatation with an increased flow. The reflex vasoconstriction to cold has been found intensified in cases of Raynaud's disease and allied conditions, feeble or absent in tabes, in well marked arteriosclerosis, the in long-standing hemiplegia, etc.) It is obvious that where anatomical changes have occurred which constitute a block on the vasomotor reflex arcs, even without obstruction of the vascular path, or a block, on the vascular path, even without interference with the vasomotors, vascular reflexes must fail to affect the blood flow through the part."

The Blood Vessels and the Blood Movement.—Two views regarding the rôle of the vascular system in the circulatory activity have found adherents in the literature. According to one of these the blood vessels take an active part in the propulsion of the blood. This presumes that the vessels pulsate actively, and propel the blood forward in a peristaltic wave, and this power is attributed not only to the arteries, but also to the veins.

According to Hasebroek¹ the pulse wave occasioned by the heart stimulates first the vasodilators, so that an active dilatation of the arteries ensues. When the pulse waves have reached the maximum, a vasoconstricting effect is aroused, and an active constriction takes place. Inasmuch as the pulse wave is transmitted from place to place towards the periphery, this stimulation and motion of the arteries is believed to take the form of a peristaltic wave, so that the blood is, as it were, aspirated during the diastole of the arteries and transmitted onward during the systole.

This view has not been acceptable to all investigators. Indeed, another school insists that the passive dilatation of vessels and the consequent re-

¹ Hasebroek, Pflüger's Arch. Bd. 168, 1917, p. 247.

bound, gives rise to the mistaken impression of spontaneous activity. These investigators, therefore, hold that the vessels play a passive rôle only.

There seems to be no doubt, however, that the vessels are active so far as certain variations in their caliber do depend upon nervous influences. Through the vasomotor system the vessels conserve a certain degree of tension or so-called tonus.

Capillary Circulation and Blood Movement.—The capillaries are prone to show rhythmic contractility following nerve stimulation. This observation is of importance for its bearing on the existence of an extracardiac force in the propulsion of blood. Fleisch¹ contends that the rhythmic contractions exhibited by the excised arterial strip does not prove that an independent extracardiac propulsive force exists.

This author calls attention to the fact that the rate of contraction of isolated arterial preparations at body temperature is less than the heart rate. If, therefore, such vascular movements occurred in the normal intact animal, they would be as likely to impede as to facilitate the force of the heart beat since they are neither synchronous with it, nor can they travel with the same rapidity over the vascular tube. He rejects the view, therefore, that the arteries furnish an extracardiac circulatory force. Whether the veins contribute circulatory power is still a mooted question. Since cinematographic records show no rhythmic change of caliber in the capillaries, the latter are probably also impotent as circulatory adjuvants.

Hooker takes exception to these views in the light of recent investigations. He states that the mammalian capillaries and venules have been shown to undergo post-mortem changes in that they are almost completely emptied of blood shortly after death. Later they fill again and subsequently and finally empty themselves. Since no extraneous forces are at work, this phenomenon cannot be passive in character both as to emptying and filling. In other words, the capillaries under these circumstances exhibit a functional response which might be of distinct moment in moving the blood under normal conditions.

In accordance with more modern investigations, it does not appear unwarranted to entertain the view that the capillaries and venules may offer an extracardiac force of very considerable significance to the circulation.

Hooker says that "up to the present, no one has attempted to show, except in the case of the bat's wing, that the veins proper facilitate blood movement by contractile activity. There is abundant evidence that the tone of the veins is an important factor in circulatory regulation and we know that respiratory, joint and muscular movements facilitate, by a massage effect, the movement from valve segment to valve segment of the blood in the large veins. The sole indication, however, that the veins may move the blood by a kind of peristaltic activity is found in analogous observations that the large lymphatic trunks in situ may exhibit spontaneous rhythmicity of a peristaltic character."

Vasomotor Function and Circulation.—To understand better the action of the vasomotor nerves, let us quote the example given by Starling² of the effect of vasoconstriction and dilatation of the arterioles of a part or organ of the body.

"If the arterioles A in the organ B dilate (Fig. 28), the first effect is a diminution of the resistance to the flow of blood into the capillaries beyond. Supposing that the arterial pressure in the trunk C remains constant, a local diminution of resistance in A will at once determine an increased flow of blood through the arterioles, and the fall of pressure from A to the capillaries will be less than when the arteriole was constricted. If the organ is distensible and elastic, the increased pressure in the arterioles and capillaries will cause dilatation of these vessels, and a consequent dilatation of the whole organ. The same effect on intracapillary pressure, and therefore on the volume of the part, may be caused by obstruction to the flow of blood from the veins. *Provided that there is no obstruction to the flow of blood through the veins*, and that the general blood pressure in C remains constant, dilatation of an organ may be taken as an expression of vasodilatation in the arteries with which it is supplied. The diminution of the resistance in A may also increase the velocity of the flow through the part, since the amount of blood flowing in a given period of time through any vessel varies directly as the difference of pressure, and inversely as the resistance in the vessel."

¹ Fleisch, Schweiz. med. Wchnschr., June 10, 1920, 323.

² Starling, *loc. cit.*, p. 989.

Vasodilatation, therefore, leads to increased circulatory conditions and a heightened velocity of blood through the parts involved. Wherever, an increased demand for local blood supply occurs, a nervous mechanism is set into action with a view to enhancing the circulation. So also an increased blood pressure will cause vasodilatation.

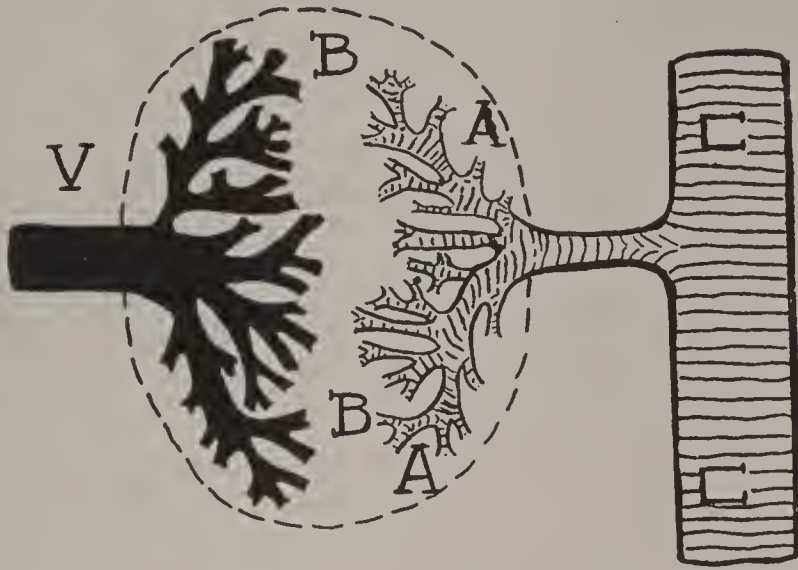


FIG. 28.—Diagrammatic illustration of physiological action of constriction and dilatation of the arteries. (Starling)

If we compare these physiological observations with the phenomenon of erythromelia described under thrombo-angiitis obliterans and arteriosclerosis, we will appreciate how an increase of blood pressure or greater demand for capacity is made on the superficial arterioles. For with so many of the deep circulatory avenues occluded and with the diminished influx to the muscles and profound parts, the tendency to fill the superficial arterioles and capillaries by way of collaterals or paths still uninvolved, must be increased. And with the rise in local pressure, an inducement to arterial expansion is at hand. To what extent neurogenic vasodilatation is responsible is not known.

The Vasomotor and Autonomic Responses.—A large number of observations tend to show that after a transitory contraction, the capillaries are prone to dilate upon the action of cold. Nägelsbach¹ observed that when the hand is put into snow, reactive dilatation of the capillaries can be observed with the Weiss² method. This author found the capillaries dilated and the circulation retarded as a result of the action of the snow compress, the color of the fingers becoming bluish, continuing so during a five minute period of observation. After the removal of the snow and drying of the fingers, the altered color and the dilatory circulation persisted about five minutes before the return to normal took place.

The dilatation of the capillaries following the action of the cold is regarded as a reactive process similar to that seen in acute inflammation and in the hyperemic reactions after the applications of a tourniquet. A similar phenomenon, elsewhere described as a reactive or reactionary or induced hyperemia or erythromelia, is noteworthy in organic vascular diseases, especially in thrombo-angiitis obliterans. Some believe that the dilatation of the capillaries may, however, be due to the direct action of the cold upon the vessel muscle.

¹ Nägelsbach, Deutsch. Ztschr. f. Chir., 160, 1920, p. 221.

² Weiss, Ztschr. f. exper. Path. u. Therap., 1918, Bd. 19, p. 390. Described in Chap. VIII.

Such reactionary conditions may occur without participation of the spinal nerves. Bier has shown that they manifest themselves in an extremity that has been wholly cut off from the trunk experimentally, a glass tube bridging the gap and providing for continuity of arterial circulation.

That the vessel nerves are not essential is deducible from the experiments of Lewarchew¹ who was able to obtain reactions in the vessels even after the electrical irritability of the cut nerve had been exhausted. It is hardly extraordinary that such independent function of the muscle fibers of the vessels exists, since the embryonic parts of certain animals are seen to contract before nerves have been developed. We may concede, therefore, that the reaction of the vessels through cold does not necessarily take place by way of nerve paths. This response in the vessels can be strengthened by adaptation to climatic conditions. The reactionary rubor in thrombo-angiitis obliterans is another beautiful example of adaptation of circulatory conditions to a new status, and also can be observed to develop as it were, under our eyes, namely, during the period of clinical observation.

The secondary vasodilatation after preliminary vasoconstriction that results from the action of cold, seems to be of teleological significance, since nourishment of the affected part is furthered by the increased flow of blood. These phenomena seem to occur most rapidly and most intensively in the exposed portions of the body. The dilatation of the capillaries diminishes the resistance in the affected territories, whilst the dilatation of the afferent arteries makes possible the delivery of a larger quantity of blood. Thus, the enhancement of the circulation adds calories to the parts, whilst the flowing of the capillary stream by virtue of their dilatation enables a larger distribution of calories to take place in the tissues. The added warmth thus acquired can be so intensive that a limb dipped in ice water may lose no more than .2° C. after almost an hour's exposure.

In anemic individuals the reaction is deficient. In keeping with this observation is the fact that anemic individuals are more apt to suffer from frost-bite. Bier has observed that in such individuals it is difficult to produce the typical red form of stasis (hyperemia) or congestion upon the application of the elastic bandage.

The changes in the tonicity of the vessels is partly of reflex origin, and so remote actions may be produced. When one arm is plunged into cold water, the cutaneous vessels of the other arm may undergo constriction; and indeed, with even a similar but less marked reaction over other parts. This phenomenon has been employed by physiologists (Stewart) in studies of blood movement in the extremities, and is often invoked as an index of the susceptibility of the vascular system to vasomotor reflexes.

The Chemical Regulation of the Blood Vessels.—Substances called metabolites produced incident to katabolic activity, may chemically stimulate the vessels themselves and increase the blood flow. Krogh believes that there is normally a hormone, possibly derived from pituitary function, that brings about a certain degree of tone in the capillaries. Here we are concerned, however, with the larger vessels.

The great enhancement of the flow through the muscles associated with muscular exercise is brought about largely by overactivity. The experimental introduction of carbon dioxide or lactic acid into the blood causes marked dilatation of the blood vessels of a limb. Carbon dioxide then, regarded as a universal hormone liberated in the circulation on general

¹ Lewarchew, Pflüger's Arch., 1881, Bd. 26, p. 60.

increase of body activity, seems to have not only a central effect through excitation of the medullary and spinal centers (causing contraction of the blood vessels), but also a local peripheral effect bringing about vascular dilatation. The total result therefore, according to Starling would be "to cause dilatation of the blood vessels of the part when carbon dioxide is produced, and where it is present in greatest concentration, and vascular constriction elsewhere under the influence of the sensitive nervous system."

How such physiological processes are deranged, can be exemplified by the ischemia that is often noted after exertion in the foot and legs of cases of arteriosclerotic disease and thrombo-angiitis obliterans. Such blanching is diametrically opposed to the functional regional demands and to the modus above described. Whether we are to presuppose a heightened irritability of the vasoconstrictor centers whose actions nullify the local tendency to arterial expansion produced by the carbon dioxide, or whether by reason of impoverished local circulation, other chemical agents counteract the expected and usual phenomena, are questions that have not as yet been solved or satisfactorily answered.

The products of tissue activity are also believed to exercise an influence on the caliber of the arterioles. Gaskell demonstrated that acids (especially lactic) may have a direct action on the arterioles, causing these to relax. Bayliss found that carbon dioxide produces a like effect. Both the latter and lactic acid result from processes of oxidation, carbon dioxide in all cellular activity, lactic acid usually in muscle. Bayliss concludes that carbon dioxide may be one of the chief chemical agents capable of bringing about increased blood supply to active tissues. However, the action of "metabolites" is in all probability aided by vasodilator nervous reflexes.

The Internal Secretions and the Circulation.—The endocrine glands have a double relation to the vegetative nervous system; and the regulation of their secretory activity is believed to be dominated by the vegetative paths in spite of the fact that the glands may functionate when all afferent nerves have been divided. Then, too, the hormones delivered into the blood paths may modify the excitability of the vegetative nervous system.

For example, the adrenals receive secretory fibers from the splanchnic; and adrenalin on the other hand, may stimulate, the sympathetic nerve endings, and in turn enhance the secretory activity of these glands.

Authors are not in accord regarding the influence of the thyroid secretion on the vegetative nerves. It probably exercises a stimulating effect upon the sympathetic and parasympathetic fibers.

It may suffice here to refer briefly to the latest theories regarding the action of *adrenalin*, the *hypophysis* and the *pituitary* bodies.

Adrenalin.—The constrictor effect of adrenalin on the small arteries, arterioles, capillaries and portal veins with the consequent increase in arterial blood pressure is well-known. This contraction has been observed after section of the cervical cord, and destruction of the spinal cord, and therefore has been interpreted as an influence acting directly upon the vascular musculature. The vasomotor centers, however, are regarded as playing a rôle by some. Although physiological observations would indicate that the normal vessel tone is dependent upon the direct action of adrenalin, this view is not in accord with the circumstance that the adrenalin action disappears rapidly; nor is it in consonance with the failure of the blood pressure to fall after bilateral exclusion of the adrenal bodies. And so others take the view that adrenalin under normal conditions conserves

the receptivity of the vessel musculature to stimuli brought to it from the central nervous system. Still others believe that under excessive demands, an abnormal amount of adrenalin is given off, and the vessel muscle is directly irritated by this internal secretion. Under such circumstances the adrenal bodies play an important rôle in the regulation of the vascular tone.

The question as to whether *adrenin* contributes under normal conditions, in the maintenance of the blood vessel tonus has given rise to much discussion. Although many believe that this substance is continually present in the blood and is a factor in the maintenance of the tonus of the blood vessels, Hoskins,¹ Vincent,² and Stewart³ are not in accord with this view.

These investigators have been unable to find adrenin in the blood stream. Furthermore, under normal physiological conditions, they believe that it has no effect on the physiologic processes. Under special strain, however, when the sympathetics are stimulated, the chromophil cells of the medulla of the adrenals are stimulated and adrenin is thrown into the blood stream. Under these conditions it may intensify and prolong the sympathetic action.

Adrenin may not always produce vasoconstriction as is generally believed. Its effect depends upon its concentration and dosage; and it may produce vasoconstriction in one set of vessels and compensatory vasodilatation in others.

Hartman⁴ states that the mechanism causing vasodilatation in the intestine, when adrenalin is injected into the general circulation, is located in the collateral sympathetic ganglia, probably in the superior mesenteric ganglion. He further believes that "in the adult, adrenalin poured into the blood in small quantities, causes by its peripheral effects, constriction of the vessels in the skin, mucous membranes, and abdominal organs, driving the blood into the vessels supplying the skeletal muscles which are actively dilated for its reception through the effect on the sympathetic and dorsal root ganglia mechanism. But as the quantity of adrenalin liberated increases, the peripheral effect begins to overcome the ganglionic effect in skeletal muscles, the intestinal vessels by action on the sympathetic ganglia begin to dilate and the blood is reversed in its path."

The rôle of adrenalin with respect to its influence on the regulatory vegetative mechanism in the corpus striatum and mid-brain (Dresel-Brugsch) is given more detailed consideration elsewhere (Chapter on Vasomotor Neuroses).

The *hypophysis cerebri* is also believed to have an influence on the circulation. A colloid substance is formed in its middle portion, which is said to extend and permeate through the infundibulum into the third ventricle. According to Schäffer two substances can be extracted out of the hypophysis, and these differ chemically. One of these produces a transitory fall of arterial pressure. The other substance is *pituitrin*, which can be extracted from the human hypophysis, and which causes retardation of the heart action. All vessels of the body, even those of the lungs and the heart may be caused to contract by the action of pituitrin. Only the vessels of the kidney are an exception, for these may even dilate. The action of pituitrin as a vasoconstrictor is more durable than that of adrenalin; but after repeated injections its effect diminishes, and may at times bring about a reduction in the blood pressure. Inasmuch as the action of pituitrin continues even after destruction of the higher vasomotor centers, it probably has a direct influence upon the peripheral vascular mechanism.

It has been recently suggested that the blood contains a substance essential for the maintenance of the contractility of the Rouget cells—those

¹ Hoskins, *Endocrinology*, 1, 292.

² Vincent, *Endocrinology*, 1, 140.

³ Stewart, *Endocrinology*, 1, 151.

⁴ Hartman, *Endocrinology*, 1918, 2, p. 1.

elsewhere described as responsible for inherent capillary activity. Experiments (Krogh and Rehberg) have sought to identify this substance with the pituitary hormone. Indeed, preponderating evidence is in favor of the existence of such a hormone that may act in a dilution equal to 1:100,000, or 1:1,000,000 of commercial pituitrin.¹ When circulating in the blood, a physiological effect is doubtless exercised on the capillaries. In view of the discrepancies in the action of pituitrin on various vessels of animals, much clarification of our present knowledge on the mechanism of capillary tonus is still desirable.

CHAPTER VII

PHYSIOLOGY OF THE CAPILLARIES²

General Considerations.—For an understanding of the visible manifestations of changes in arterioles and capillaries in deranged circulation of the extremities, it is well to review certain elementary facts regarding capillary circulation.

1. The total number and volume of the capillaries is enormous as compared to that of the arterioles.

2. The rate of flow is greater in the arterioles than in the capillaries.

3. Pressure on the arterial side must needs be markedly increased whenever the caliber of the arterioles becomes diminished; for here the flow is rapid and friction is proportionate to velocity.

4. The importance of variations in size of the capillaries can be well understood if we consider that but slight dilatation over a large area may cause accumulation of a large amount of blood.

Recent observations in the normal state of the capillaries and their responses to various stimuli are illuminating and open a new vista of thought in explanation of signs of obstructed peripheral circulation.

Normally, a relatively small number of capillaries in the muscles is filled with blood (Krogh). Muscular activity alone suffices for the dilatation of the collapsed capillaries. Nature would not adequately play her rôle did not the arterioles, too, enlarge commensurately. For, with dilatation of capillaries *alone*, the total blood supply would be hardly augmented, and stasis in the dilated capillaries with defective oxygenation occurs. With contracted arterioles the stagnation would be intensified.

From these physiological facts we would infer that a *disharmony in the reciprocal functional activities of arterioles and capillaries may be responsible for some of the clinical evidences of disturbed cutaneous circulation.*

But an *independent activity of the capillaries* plays an important part both under normal and pathological conditions. Whilst the arterioles may contract synchronously with the capillaries as upon the action of cold, they may manifest opposite motility.

When the skin is hyperemic, red and warm, the flow through the capillaries is enhanced and the arterioles are simultaneously dilated. This is a defense mechanism of nature against cold and other insults.

When the skin is cyanotic or bluish, it is usually cold, the supply of blood impaired, oxygenation diminished and the current of blood retarded.

¹ Parke, Davis & Co., pituitrin from the posterior portion of the pituitary.

² For deductions based on capillary microscopy the reader is referred to Chap. CVI.

Here we must assume opposed activities—the arterioles constricted, the capillaries open or dilated. It is conceded to-day that these structures are capable of active alterations in caliber.

The fact that capillaries consist of but a single layer of protoplasmic cells and are devoid of a muscular coat does not preclude active changes in their caliber, since we know that cells other than muscle can undergo alterations in form under stimulation. More recently, however, powers of contractility have been relegated to certain other elements in the capillary walls (Vimtrup and Krogh). Rouget in 1873 described strongly branched contractile cells lying on the outside of the endothelial walls, sometimes almost completely encircling the capillaries. Latterly it has been shown that the contraction of capillaries begins at one or more of these cells. Their function is believed to be that of altering the lumina.

The Autonomic Action of the Capillaries.—Clinical observations on the variations in color tints that may occur in many of the neurogenic forms of the vascular maladies have often aroused the doubt that pathologic nerve impulses alone could explain the phenomena. Let us recall the evanescent mottling of red, white and bluish black that may come and go in certain cases of thrombo-angiitis obliterans, particularly when the affected part is unclothed in a warm room after exposure to the cold; and let us call attention to the play of colors and the variegated mottling in patches of indeterminate shape and size that are characteristic manifestations in some of the cases of vasomotor instability and Raynaud's disease. Such multiform evidences of capillary activity or passivity, corresponding to no known areas of vascular or even nerve distribution, have oft awakened the thought that neither purely mechanical, obstructive or neurogenic influences offer adequate explanation.

Leaving out of consideration the rôle of the pumping mechanism, and reviewing the peripheral factors in the blood vessels themselves, we have been taught that vasomotor influences are for the most part responsible for the alteration in peripheral resistance, and the quantitative distribution of the blood into the tissues. Physiologists have relegated the functional vessel control to the vasoconstrictor and vasodilator nerves that are said to act in the arteriole walls. It has been conceded, too, that because of a certain sensitiveness on the part of the vessels and the products of cellular activity, and possibly exogenous toxins too, local vascular changes in volume might be the result of the action of metabolites and hence not be altogether dependent on nerve control. Hooker,¹ believes that capillaries can dilate or contract independently of the larger vessels with which they are continuous. The capillaries and venules are thus regarded as able to furnish peripheral resistance as well as the arterioles. Hooker concedes the rôle of chemical factors as influencing the peripheral circulation. He thinks that, as a rule, there is a harmonious interrelation of the activity of the higher nervous control and the primordial autonomic (possibly chemical) regulated forces possessed by the smallest vessels.

For an understanding of this more modern view regarding the activities of the capillaries and *their responses to both nerve and local chemical influences*, some of the observations and researches that have led up to the acceptance of autonomic activity may be worthy of mention.

The facts that have been experimentally adduced may be summarized as relative to:

1. Nerve control of capillaries and venules; and

¹ Hooker, Am. Jour. Physiol., 54, 30, Nov. 1, 1920.

2. Direct influences on capillaries, arterioles and venules. This second group of possible motivating agents is again divisible into

(a) Direct mechanical stimuli; and

(b) Direct chemical (metabolic, katabolic) stimuli.

The clinical data in support of the newer concepts will be discussed separately wherever the diseases or manifestations of deranged peripheral vascular function seem to have a bearing on the hypotheses here expressed.

1. The Nerve Control of the Capillary Circulation.—In the theory of capillary function, the effect produced by nerve stimulation is the cardinal factor. Sectioning and stimulating the cervical sympathetic in the cat produce at first a cessation of corpuscular flow, due in all probability to arteriolar constriction. The corpuscles then begin to clump and move forward in an irregular fashion, so that in the relatively brief time that the electrical stimulus is continued, the corpuscles disappear from the field of observation. Immediately after cessation of the stimulus, however, the appearance of corpuscles from the arterial side is again noted in more profuse flow than before. This phenomenon can be obtained successively on the same preparation without any indication of fatigue, evincing conclusively that the capillaries and venules are subject to nervous control.

Still other experiments (Krogh) on the capillary responses to punctiform trauma of the frog's tongue have demonstrated that stimulation of sensory nerve filaments may result in capillary dilatation; and this by way of a sensory vasomotor nerve reflex in an antidromic direction.

It is generally conceded to-day that epinephrin acts only on tissues with sympathetic innervation. If 3 cc. of a 1:50,000 adrenalin solution be injected intravenously, the action of the capillary bed is similar to that in nerve stimulation, in that there is a cessation of the corpuscles, clumping, with gradual and irregular movement out of the field. It may be accepted then that the observations here described are directly dependent upon a functional response of the endothelium.

Recent observations also point to a regulatory nerve mechanism in the case of the veins.

Peripheral Venopressor Mechanism.—Venous pressure may be caused to rise¹ in the sigmoidal area of the large intestines in dogs, isolated except for its nervous connections via the inferior mesenteric ganglion. After washing out the blood by perfusion, the artery was left open and the drainage vein connected with a water manometer. A rise of pressure of 7.5 cm. of water followed direct electrical stimulation of the nerve to the part; indirect stimulation (asphyxiation) acting by way of the medulla gave a rise of 4.5 cm. of water. A possible action of the intestinal musculature was excluded by coincident records of the pressure within the lumen of the gut itself. Hooker records as follows "the results thus obtained were regarded as substantiating the existence of a central as well as a peripheral venopressor mechanism. Whether the contraction was in the larger vein, in the venule or in the capillary, or in all of them together, was not possible of determination, but it was believed that the arteriole and artery were effectively excluded. In our present knowledge we should probably emphasize the participation of the capillary and venule although the direct evidence is not at hand in this particular experiment."

Briscoe² made a careful study of the venous and capillary pressures in the cyanosis of the hands associated with "irritable heart." A special apparatus was used; with it the collapse of the superficial veins was regarded as criterion for venous pressure, and the blanching of the skin under the glass capsule as indicative of capillary pressure. Throughout the observations the venous pressure was found within normal limits (average 11.4 cm. H₂O). The capillary pressure was, however, uniformly high and sometimes as high as twice the normal. The average capillary pressure for the controls was 23.5 cm. H₂O, and for the subjects with well marked blue hands 36.9 cm. H₂O. In these cases there is little doubt of capillary stagnation; the blue color, the tendency to perspire, the dark color of the

¹ Hooker, Am. Jour. Physiol., 1918, XLVI, 91.

² Briscoe, Heart, 1918, VII, 35.

blood, which exudes from a skin prick, all point to this condition. She states that the stasis might be due to arteriolar constriction; but that this factor may be excluded on the ground that the capillary pressure is too high. *The only mechanism which could develop such high capillary pressures with an engorgement accompanied by a normal venous pressure, would be a constriction of the venules, and this is the explanation which Briscoe proposes.*

The Sympathetic Innervation of the Capillaries.—Since electrical stimulation of the cervical sympathetic is followed by marked constriction of the capillaries in the skin of the cat's ear (Hooker); and in light of similar effects in the capillaries of the frog's web after excitation of the lower sympathetic ganglia (Krogh, Harrop, Rehberg), the influence of the sympathetic nerve mechanism has been definitely proven. Indeed, contractions are believed to start from the sites of the nuclei of the capillary contractile cells (Rouget), the latter being probably directly supplied by nerve fibers.

2. The Direct Response of the Capillaries. (a). *To Mechanical Stimuli.*—Cotton, Slade and Lewis¹ in a study of the subject of dermatographia as exhibited in soldiers with "irritable heart," showed that some of the conditions observed seem attributable to a contractile function of the capillaries. They regard the red line of the *tâche* and the flush, which may surround it, as due to arteriolar dilatation which floods more blood into the capillary bed. The white *tâche* and the white area beside a red *tâche*, however, are believed due to capillary constriction.

The spontaneous activities of the capillaries are most clearly attested by those experiments in which the blood flow in an arm was completely shut off by a supra-systolic pressure in a sphygmomanometer cuff. With the cardiac factor thus excluded and with the arm held horizontally at the time this pressure was applied, the color of the skin remained normal and the stroke of a blunt instrument developed a white *tâche* just as distinct as under normal circulatory conditions.

Since this reaction could be obtained at any time during 10 minutes of applied pressure, Cotton and Slade assume a stabilized pressure in the vessels. If under such circumstances the capillaries empty themselves of blood on appropriate stimulation, the result cannot be ascribed to arteriolar constriction and must be due to a response on the part of the capillaries themselves. Under the same conditions stronger mechanical stimulation of the skin produced a red *tâche* which was assumed to be due to a capillary dilatation, thereby permitting blood to enter from the larger neighboring vessels.

Employing the same procedure and with the larger channels compressed, these authors found that the cutaneous injection of a few drops of 1:30,000 adrenalin causes a localized pallor, much as is the case when the substance is injected with circulation intact. With the blood flow in the large vessels shut off, the pallor is said to be due to an effect exerted upon the capillaries directly.

(b). *To Chemical Stimuli.*—Krogh² states that in the resting muscle many capillary channels are occluded; and that following activity the number of patent capillaries is enormously increased. The katabolic products of muscular activity are responsible for this capillary response. This author points out how fallacious is the older view that "the number of functioning capillaries in any tissue depends upon the tension of blood in the arterioles, and that as this tension rises more and more, capillaries open up as if their tonicity varied in degree from capillary to capillary." For if this were so, the blood would tend to follow certain fixed paths when the pressure was low, and as a result, some cells would be well supplied with oxygen, while others would be in constant danger of suffering oxygen want. According to the recent views³ the capillaries are susceptible to chemical stimulation; and the blood may be deflected from one set of channels to another according to the tissue needs of their environmental cells, without changes in arteriolar pressure.

¹ Cotton, Slade and Lewis, *Heart*, 1917, VI, 227.

² Krogh, *Jour. Physiol.*, 1919, LII, 409.

³ Hooker, *Loc. cit.*

Danzer and Hooker¹ found "that one of the annoyances in determinations of capillary blood pressure in man, when the criterion employed was the cessation of corpuscular flow, lay in the fact that often the large and conspicuous capillaries were filled with stagnated corpuscles, and they noted that in the course of observations it was not uncommon to find that a previously stagnated vessel had become patent and that on the other hand, patent vessels became stagnated. Furthermore, they found under varying experimental conditions that the pressure might rise or fall in one capillary while the pressure in its neighbor remained constant or changed in an opposite direction. The structural conditions of the vascular bed are undoubtedly such that in the vast majority of instances neighboring capillaries are supplied by the same arteriole. Variations in neighboring capillaries such as have been noted, therefore must be due to inherent and independent changes in the vessels themselves." Perhaps many of the so-called vasomotor phenomena in organic vascular disease can be also thus explained.

Krogh states that capillary tone is not only independent of the blood pressure but that the spreading of the effects of stimuli is due to axon reflexes which are probably conveyed along sensory fibers. This view is in accord with the conception of Bruce² and of Bardy³ that inflammatory processes resulting from the application of local irritants are essentially due to axon reflexes. According to Krogh the capillary tonus is not of nervous origin, but must depend upon some constituent of the blood, and this constituent is not oxygen.

Paralytic Action of Poisons on the Capillaries.—Heubner⁴ has shown that the intravenous injection of the double chloride of gold and sodium produces a shock-like prostration accompanied by a remarkable engorgement and stasis of the capillaries and veins. Post-mortem examination in the case of mammals showed distended and conspicuous veins which could be traced as fine twigs to the surface of the intestine. The peritoneal surfaces were injected, and a similar hyperemic appearance of the mucous membrane was noted. Microscopically all the tissue exhibited extensive dilatation of the venules and capillaries, and not infrequently ecchymotic areas. The small arteries everywhere were strongly contracted, usually with completely occluded lumina.

Dale, theoretically and experimentally reached the conclusion without observation of the vessels concerned, that histamine is a capillary poison producing an effect upon the general circulation analogous to that established by the injection of gold salts. Cannon⁵ had previously presented evidence that the capillaries are packed with red cells in wound shock, and postulated this condition of "exemia" as the causative factor in the condition. This conclusion Rich⁶ and Hooker⁷ confirmed. Rich developed a method by which instant fixation of the omental tissues in situ could be obtained. He was then able to study the vascular picture microscopically after the omentum had been removed and spread upon a slide. Preparations made in this manner at various times after the intravenous injection of histamine in cats, and controlled by specimens in which physiological salt solution was injected, gave clear evidence that an immediate effect of the histamine was to greatly increase the number and size of the capillaries.

In photographs of the capillaries of the cat's ear, Hooker has shown that histamine causes a profound dilatation of the capillaries and venules. Though the latter believes that the vessels of this area may be less sensitive than in the omentum, he frequently observed that the dilatation due to histamine was preceded by a period of constriction. This constriction was usually fleeting in character, and while of considerable moment in regard to capillary function, is not to be regarded as disputing the hypothesis of histamine action under discussion.

Histamine does not abolish arterial vasoconstriction upon sensory nerve stimulation. It does, however, completely depress the response of the capillaries and venules to peripheral nerve stimulation, indicating again its potency as a poison for the capillary endothelium.

Summary of the Function of the Capillaries.—The significance of a thorough knowledge of the functions of the capillaries in the extremities will be appreciated when we recall that they are still patent when large vascular territories are occluded; that, though collaterals may step in to substitute for the large channels, the capillaries are essential for the delivery of oxygen

¹ Danzer and Hooker, Am. Jour. Physiol., 1920, LIV, 96.

² Bruce, Quart. Jour. Exper. Physiol., 1913, VI, 339.

³ Bardy, Skandinav. Arch. f. Physiol., 1915, XXXII, 198.

⁴ Heubner, Arch. f. exper. Path. u. Pharm., 1907, LVI, 370.

⁵ Cannon, Jour. Am. Med. Assn., 1918, LXX, 611.

⁶ Rich, Jour. Exper. Med.

⁷ Hooker, Am. Jour. Physiol., 1920, LIV, 30.

and nutritional elements, as well as for the transportation of the waste metabolites, and that functional impairment of these, too, may bring about morbid processes.

The preponderance of evidence today, leans to the view that the capillaries are not merely passive agents in which the blood flow is determined by the state of the supplying arterioles and the vessels that drain them. On the contrary, an inherent power of contractility and dilatability that actively influences the distribution of blood, is assumed to exist.

Indeed, it has been suggested¹ that paralysis of the capillaries with consequent dilatation and stagnation of blood is demonstrable in "shock." Hooker has shown that histamine produces a similar paralytic action upon the capillaries. Small doses, when injected, produce a rise in blood pressure due to the contraction of the small arterioles. With larger doses, a primary rise in blood pressure soon yields to a marked fall with a consequent condition resembling "shock." This is seen to be due to the fact that the capillaries become paralyzed and dilated with stagnation within them, thus rendering the arteriole contractions ineffective.

To what extent the functional derangement of the capillaries is a factor in nutritional disturbances accompanying the obstructive and neurogenic vascular affections of the extremities, is still a matter of conjecture.

The capillary bed can adapt itself to local tissue needs by dilatation when tissue conditions tend toward asphyxiation, by constriction when such local needs have been satisfied. The mechanical alterations in the surrounding tissue produces a variety of fluctuations in the girth of the capillaries. The corpuscles disappear from the capillary lumen when the capillaries contract and, per contra, the cutaneous capillaries may be overfilled with these elements.

It may be admitted then, in the present state of our knowledge, that both chemical and nervous influences may regulate the activity of the capillaries. For the nervous mechanism constricting effects have been observed; and, in animal experimentation, sensory, vasomotor, antidromic reflexes causing dilatation follow trauma.² Chemical factors are said to bring about dilatation of the capillaries and venules. Perhaps then in consonance with the altered chemical constituents of the surrounding fluids and tissues, and with the exigencies of special metabolic stresses, a mechanism is at hand which automatically meets local demands. Hooker, therefore, believes that we may regard the nervous control as a force tending to restrict the capillary beds over the body as a whole, thus maintaining a tone which is played upon by chemical factors.

Furthermore, since he accepts the existence of capillary and venule function in areas beyond that of the distribution of the arterioles, we must modify our conception of peripheral resistance, which heretofore had been restricted to the arterioles, the latter governed by nervous and chemical influences.

In the case of the venules also, recent investigations have brought to light data that speak strongly in favor of independent functional activities. Some of the clinical confirmatory evidences will be described later. Studies of the peripheral asphyxias would also seem to furnish corroborative testimony.

Although much has been written regarding the vasodilating effects of *acid metabolites* in active organs, more recent authors do not accept the conclusion that increased blood supply is due either in main or exclusively to the action of such metabolites. It is conceded, however, that metabolic products resulting from activity have a dilator effect upon capillaries, even though the action is not dependent on their acid properties.

¹ Dale and Cannon, Hooker, *Physiol. Reviews*, 1, 112, 1921.

² See Chap. V. Recent Views on Physiology.

The exact rôle of *adrenalin* in the maintenance of capillary tonus is still a matter of discussion; some ascribe an important part to this internal secretion (Dale and Richards), whereas others (Krogh) see in the pituitary activities the source of tonic influences for the capillaries.

CHAPTER VIII

METHODS OF INVESTIGATING CAPILLARY CIRCULATION¹

Although the capillary territory occupies the longest part of the circulation time, relatively little is known about capillary dynamics. It is true that the hydraulic principles, by virtue of the implication of many other coefficients, can hardly be wholly accountable for the flow and its aberrant clinical manifestations. And so, in estimating the several factors that are determinants of capillary flow exclusive of the cardiac pump and general vascular tone, we must take into consideration the important rôles that osmosis, absorption, cellular activity, and surface tension may play in this territory.

The Lombard Method.—Lombard described a method of studying the human capillaries directly under a microscope. He applies a drop of glycerin or castor oil to the skin, and then observes this area through a microscope with a magnification of about 75 diameters. The capillary loops in the skin can be readily visualized and studied with a strong light thrown upon the area to be examined. The capillaries are seen as comma-shaped loops but the circulation within them escapes closer observation. At the base of the finger-nail or toe-nail, where the papillae of the skin are flattened out, they appear as long, horizontal, hair-pin shaped loops, in which the blood flow can be observed.

Our investigations may take these directions all with a view to estimating capillary circulation; (1) the study of the morphology of the capillaries; (2) the character of the blood flow; and (3), the appraisal of the blood pressure within the capillaries by means of special instruments (Danzer and Hooker).

The last is a small transparent air-chamber connected with a mercury manometer, by means of which pressure can be exerted on the skin, while the capillaries are kept under observation through the microscope. According to Boas the pressure is at first raised to the point at which the capillary flow ceases; and the reading is made at the point at which the capillary flow reappears after release of this pressure.

We may briefly quote from these authors as to their observations in a field that promises much, rather in a prognostic than in a diagnostic way. Perhaps, however, certain criteria will be deduced from future investigations that may be of service in differentiating the vasomotor vascular neuroses from those early cases of obstructive vascular disease of the extremities, that are at times difficult to recognize.²

Fluctuations under varying pressures are then recorded as the circulation is intermittently arrested. The figures given are, pressure of 60 to 70 mm. for the small arteries, 15 to 20 mm. for the small surface veins, and the average for the capillaries 40 mm. Allbutt quotes von Kries as finding lower

¹ For more recent work on this subject "Capillary Microscopy" see Chap. CVI.

² See Chap. CIV (Borderline Cases).

estimates, as, for instance, 20 to 30 mm. of mercury in the capillaries. A reduction must needs occur in the smallest capillaries, and the above findings may represent rather the values in the intermediate arterioles. And so, 10 to 20 mm. is regarded by many as being more accurate.

The Müller-Weiss Method.—Most interesting data can be obtained if we study the capillary circulation in accessible parts of the fingers with proper illumination and magnification. The horizontally placed capillary loops at the base of the finger nails, according to Müller and Weiss¹ give valuable and interesting information concerning normal and pathological capillary flow.

The finger of the case to be observed is placed under the microscope, the region just proximal to the root of the nail being selected. The area immediately under the lens is covered with a drop of cedar oil that also fills out the nail furrow. Observation is made with the Leitz objective A, or a Leitz objective No. III (ocular No. 2 with about 40 diameters enlargement). The source of illumination is a strong electric lamp with a central illuminating filament (about 200 c.p.), whose light is thrown upon the object with a convex lens.

When the capillary layer and epidermis pass over into the subungual space gradually, the capillary loops are more or less horizontally placed and easy to observe. However, if the epidermis makes a steep decline under the nail, annoying light reflexes are apt to take place which can be obviated to a certain extent if a cover slip is placed over the area covered with oil immersion.

Under normal conditions the flow in the capillaries is rapid, continuous, and quicker in the arterial than in the venous limbs of the loops. The little experienced observer may have difficulty in recognizing the flow because of its rapidity.

Variations of Capillary Flow.—A number of factors influence the capillary flow. In the winter or in cold weather the flow is retarded in the narrowed capillaries, whilst in the summer and in a warm room, the flow is accelerated in the dilated capillaries.

In the vasoneuroses deviations from the normal are recorded. In acrocyanosis the flow may be so retarded that stagnation occurs. In hypertonic conditions there is a pulsatile flow, and in aortic insufficiency, a true capillary pulse can be observed.² In arteriosclerosis, there is a slowing and dilatory type of current, with marked insufficiency of the circulatory system, characteristic diminution in the rapidity of the flow is observed; even to the extent of complete stasis in the dilated venous limbs of the capillaries. Or spontaneous reflux from the venous into the arterial limb may take place. Such observations must be regarded as of some prognostic import.

In order to exclude the cardiac factor, Weiss and Dieter³ did experimental work in which the vascular territory examined was suddenly excluded from the heart action. Observations thus made were described as applying to a closed vascular territory.

Capillary Circulation in a Closed Vascular Territory.—Weiss and Dieter's studies were carried out as follows. The circulation of an extremity was suddenly brought to a stand-

¹ Weiss, (a) Arch. f. klin. Med. 119, 1-38. (b) München. med. Wchnschr., 1916, 925. (c) München. med. Wchnschr., 1917, 609. (d) Wien. klin. Wchnschr., 1918, 41. (e) München. med. Wchnschr., 1918, 607. (f) Ztschr. f. exper. Path. u. Therap. 19, 390 (1218). (g) Ztschr. f. ärztl. Fortbild., 16, Nr. 7 (1919). (h) Reichsmedizinalanzeiger, 44, Nr. 1 (1919).

² This is not in accord with the views of other authors.

³ Weiss & Dieter, Zentralbl. f. Herz. u. Gefasskr., Dec., 1920, p. 295.

still with the use of a pneumatic blood pressure cuff, the previous, coincident and subsequent condition of the capillary flow being included in the investigation. In order to avoid over-filling of the venous territory, a sudden increase of pressure in the cuff was attained by the use of a cylinder of compressed oxygen connected with the blood pressure apparatus.

After the application of the cuff, selected capillaries are placed into the field, with two investigators put in charge. The first observer takes note of the flow in the capillary loop, whilst the assistant manipulates the Riva-Rocci (blood pressure) and the oxygen apparatus. At the command of the first observer, the cuff is suddenly distended so as to obtain a maximum pressure (about 200 mm. of mercury). As the mercurial column rises, a stop watch is started.

When the capillary flow ceases, a signal is given to the second observer who times this moment. The first observer is not permitted to waver in his watchfulness of the phenomena in the capillary loop, the assistant taking full charge of the time calculations.

In normal persons at ordinary room temperature, the duration of the capillary current is 30 seconds. A longer continuation of the flow is caused by equalization in the pressure in the arterial and venous systems. At a colder temperature the time of flow is shortened by increased tonus and contraction of the vessels. At a higher temperature it is increased by dilatation and relaxation of the vessels and there is a back-flow of the blood from the venous limbs of the capillaries into the arterial limbs. After plunging the hand momentarily into ice water, the time is shortened at first, but after the passing of the reaction it is lengthened.

In benign nephrosclerosis with marked hypertension there is lengthening of the time of flow as a result of the marked difference in pressure between the arteries and veins. Back flow may take place on account of the high tonus.¹

Although but few observers have as yet made use of this procedure, it is well worthy of an extended trial. Some deductions of value may be expected in the early cases of vascular occlusion, when objective manifestations are not as yet sufficiently distinct to allow of certain diagnostic conclusions. Whenever we wish to make inferences regarding the existence of localized vascular derangements of function, however, the influences of the general systemic circulation with the heart action, must necessarily be excluded.

(1) *The Morphology of the Capillaries.*—The normal appearance of the capillaries at the base of the finger nail is shown in Fig. 29. Here are one or two rows of simple loops just proximal to the cuticle, and below them many rows of shorter, comma-shaped vessels are seen. In the first row the papillae of the skin are flattened out so that the vessels are viewed running horizontally, while in the lower layers, where the papillae are present, only the tops of the vertical capillary tufts come to view. In the present state of our knowledge we cannot generalize and accept certain capillary pictures as pathognomonic of a certain disease (Boas). It appears, however, that whenever the vascular system is affected, the capillaries suffer visible alteration, and that this change manifests itself chiefly in an increase in length and tortuosity of the vessels.

This author compares the capillary changes to similar ones in the arteries. "Disease of the arteries exhibits itself to the clinician either as a thickening of the vessel wall, or as an increase in length and increase in tortuosity of the artery. The tortuosity is consequent on the lengthening of the vessel, since the distance between the origin and termination of the artery remains the same, an increase in length must manifest itself by a greater twisting and curving of the vessel." Anything that tends to increase the length of the capillaries, will tend to bring about looping. Two chief factors are possible etiologic agents. One is an alteration in the capillary wall itself, and the other is a loss of tone due to abnormal nervous control. Thus both

¹ Weiss and Dieter, *Loc. cit.*

organic vascular disease, as well as imperfect nervous control (as in vasomotor instability), may bring about structural alterations in the capillaries.

(2) *The Blood Flow in the Capillaries.*—There is uniform filling of all of the vessels in the microscopic field, and only after a close study will the streaming of the blood become apparent. The flow is rapid and constant and never pulsatile, and the blood column in the capillaries is a continu-



FIG. 29.—Normal capillary picture. (Boas)

ous one. A vessel may be seen in which the flow is sluggish at times, only to quicken in a few moments. No pulsatile flow occurs in the capillaries. Cold will retard the flow, while heat will accelerate it. When the capillary flow becomes slow, the column of blood no longer has the normal continuous and uniform appearance, but is broken into segments separated by colorless areas. This may be called a “granular streaming.” It is rarely observed in the normal circulation, and when present in many capillaries, indicates some disorder of the capillary circulation. The flow of the blood in the capillaries may be artificially modified either by inflating a blood pressure cuff that has been applied to the arm, or else by inflating the capsule of Danzer and Hooker’s microcapillary tonometer. Under such conditions, the capillary circulation may be altered at will, and the variations in the flow may be studied at leisure.¹

In acrocyanosis (Fig. 30) the capillaries are longer and more tortuous than usual and may present quite a bizarre shape. With this it will be observed that during the period in which the hands are cold, there is complete stasis in many of the vessels, and in the others the flow is sluggish and

¹ Boas, *Loc. cit.*

irregular. The blood pressure in these capillaries is very low. Immersion of the hand in hot water provokes a remarkable change. The hand becomes bright red. Under the microscope we see the blood streaming rapidly through the capillaries, and all signs of stasis have disappeared. At the same time the capillary blood pressure has risen to a normal figure.

The following observations were made in cases of thrombo-angiitis obliterans by Boas. It was noted that but few capillary loops were visible.



FIG. 30.—The capillaries of the finger in a case of acrocyanosis. (Boas)

After rubbing the area of skin under observation with a blunt instrument, many anastomosing and branching capillaries came into view. These observations lend themselves to the interpretation that many of the capillaries were tightly contracted, permitting the passage of no blood until the mechanical stimulus brought about their relaxation.

Spasms of the capillaries have been observed in Raynaud's disease (Halpert¹). During an attack, although the number of capillaries visible remain unchanged, the larger capillaries become fuller, especially their venous loops, and their contour changes. In severe attacks the capillary flow ceases; but in the larger capillaries the blood is pushed through the vessel in a peristaltic-like wave. Pribram and Henius describe a similar peristalsis of the capillaries in the stage of ischemia.

(3) *The capillary blood pressure* can be estimated with Danzer's and Hooker's microcapillary tonometer. The part is kept at heart level during the test in order to avoid the hydrostatic effect of the column of blood. The figures given are 15 and 30 mm. of mercury for normal individuals. Read-

¹ Halpert, Ztschr. f. ges. exper. Med., 11, 125, 1920.

ings, however, may vary with the finger examined. According to recent observations the variability has been on the average 18 mm. Absolute figures cannot be given. It is said that when the readings tend to be above 30 mm. Hg., the capillary pressure is high; when they are below 15 mm. Hg., the pressure is low.

The Results of the Tests.—Recent observers have studied the capillaries in acrocyanosis from the morphologic standpoint, in regard to the character of the blood flow, and also as to the capillary pressure. The method of Danzer and Hooker is recommended for capillary blood pressure estimations. These authors describe a microcapillary tonometer by means of which estimations can be carried out with some accuracy. A practical, convenient technic was developed. The principle was introduced, to wit, that the cessation of the blood flow in the capillaries, rather than the disappearance of the capillaries marks the proper pressure at which the reading should be taken.¹

They found that the normal capillary pressure ranged from 18 to 22 mm. of mercury; but that in any individual most of the readings on different capillaries varied from 6 to 7 mm. of mercury although in many capillaries the difference was greater. They, however, discarded the very high and the very low readings and took as the capillary blood pressure the average of those which did not exceed this variability.

Boas² in a personal communication reports that he had examined 12 patients who exhibited *acrocyanosis* of various forms from the mildest to the more severe degrees, employing the technic of Danzer and Hooker, except that the finger of the patient was not scrubbed for fear of introducing a complicating factor.

Although the cases examined by this author, and some of those who are to be quoted as applying these newer procedures for the study of the capillaries are referred to as “acrocyanosis,” they may not truly belong to the group we have elsewhere discussed.³ All that can be said is that cyanosis of the peripheral parts was doubtlessly present.

The capillary blood pressure was found low in every case. He says that the normal capillary pressure as determined by this method, varies from 20 to 30 mm. Hg., and that another striking feature is the lack of variability of the capillary pressure. In patients with normal or high capillary pressure, the individual readings made on different capillaries usually show a variation of about 20 mm. Hg. “The capillary pressure in 10 readings registered 2 or 3 mm. Hg., and on 1 capillary only was a reading of 17 mm. obtained. The cold hand was then immersed in very hot water, and became bright red in color. The capillary pressure taken immediately was from 19 to 20 mm. As the hands slowly cooled and again became pale and blue, the readings dropped first to 13 and then to 8.5 mm. It was striking, too, to observe the change in the blood flow in the capillaries. When the hands were cold and blue, the streaming was very sluggish and irregular, but after the hot water bath it became very rapid and the capillaries became full.”

From these observations the author concludes, that when the hands are cold and cyanotic, the capillary blood pressure is low and the flow sluggish. According to his view this cannot be due to a constriction of the venules, but must depend upon a constriction of the arterioles or a marked dilatation of the capillaries. It is significant, too, that the capillaries become fuller when the hands become warm. If the venules were constricted, the capillaries would be engorged during the period of cyanosis.

Regarding the morphology of the capillaries in acrocyanosis⁴ Weiss noted that in patients of an asthenic build, who often exhibit acrocyanosis, the capillaries are more tortuous than normal, particularly in the venous portion, and that the blood stream is slow and may even at times be completely arrested. “In the vasoneuroses he saw contractions of the arterial limb of the capillaries in ischemia and a dilatation of the venous limb when the hands became

¹ For a critical survey of methods to determine capillary pressure see Friedenthal, *Ztschr. f. exper. Path. u. Therap.*, 19, 2, 1917.

² Boas, *Studies from Montefiore Hospital*, 1922.

³ Chap. XCV (Chronic Acroasphyxia).

⁴ Note that the term “acrocyanosis” as used here, is a more general designation for a cyanotic condition of the peripheral parts.

blue. The appearance of the capillaries, as well as the speed of the blood stream, may vary from moment to moment. Warming the hand accelerates the blood flow in the capillaries. Mertz¹ found long and tortuous capillaries in children with vasomotor instability. Parrisius² observed a movement which he likened to peristalsis in the venous arm of the capillaries in a patient with local asphyxia of the feet. This caused an interruption in the continuity of the blood column. He also noted changes in the form of the capillaries in the vasoneuroses. In a case of Raynaud's disease Weiss saw very wide capillary loops, which exhibited variations in caliber. In a similar case Pribram and Henius³ observed a capillary spasm associated with the ischemia. Halpert⁴ described in detail the capillary changes in a patient with a typical Raynaud's syndrome. She found increased tortuosity of the capillaries, as well as groups of capillaries 3 to 5 times larger than normal. The blood flow was slow. During an attack the giant capillaries became fuller, especially in their venous portion, and exhibited changes in contour, such as projections and strictures. The blood appeared to be pushed through the vessel by a peristaltic-like wave. In a severe attack the blood became completely stagnant and blue."

Léris and Pollicard point out that in Raynaud's disease the capillaries may become almost invisible as the integument becomes blanched. The lateral branches of the capillary loop become filiform, whilst the summit of the loop may remain unchanged enclosing the retained blood cells. Only slight reduction in the lateral branches may occur in the mild attacks. After the crisis is over, dilatation of the whole capillary loop occurs.

These authors conclude that besides arterial spasm, capillary spasm occurs in Raynaud's disease. The subsequent capillary dilatation may be explained on the theory of the action of chemical metabolites (humoral theory) according to which accumulating toxic products resulting from poor oxygenation and metabolism produce diminution in the tonus of the capillaries.⁵

CHAPTER IX

GENERAL CIRCULATION UNDER PATHOLOGICAL CONDITIONS⁶

From a study of the function of the peripheral vessels, many of the pathological phenomena observed in the diseases of the vessels of the extremities will be better understood. The task of the vessels is to deliver to any organ or part of the body the necessary quantity of blood. This necessitates a normal functional activity of these channels. The requisite quantity adapts itself essentially to the needs of such oxygenation as may enable tissue respiration to go on. The aim is to deliver nutritive substances, and to take away products of metabolism. The need for oxygen seems to be the motivating factor in the functioning of the vessels. The physiological activity of the vessels is of reflex nature.

¹ Mertz, *Deutsch. med. Wchnschr.*, 46, 480, 1920.

² Parrisius, *Pflüger's Arch.*, 191, 217, 1921.

³ Pribram and Henius, *Berl. klin. Wchnschr.*, 57, 67, 1920.

⁴ Halpert, *Zeitschr. f. ges. exper. Med.*, 11, 125, 1920.

⁵ Since the above was written further researches have warranted the inclusion of additional data summarized in Chap. CVI.

⁶ The derangements of the circulation following peripheral nerve lesions are described in Chap. XCI.

Disturbances in the mechanism can arise, firstly, through paralysis of the vessel muscle, with consequent dilatation of the vessel and loss of the regulatory influences; and secondly, through rigidity of the vascular walls of organic nature preventing adaptation of the lumen of the vessel to the requirements or diminishing the degree of response.

Vascular Insufficiency.—When either of the above conditions obtain, we may speak of vascular insufficiency. In other words, loss of tonus or increased tonus is responsible for impairment of the work of the vessels, and may lead to insufficiency of these. Palpation of the pulses gives but a limited notion of the tonus, permitting us to differentiate between hard, soft, dicrotic pulse, etc.

A distinction has been made between an active or passive hyperemia of organs, or of the skin. The power of adaptation or response of the vessels to thermic irritants (cold or warmth) depends upon the intactness of the essential vasomotor nerve functions. Exercise or muscular exertion with its attendant demands on the muscle tissues will normally effect dilatation of the afferent arteries, with increased rapidity of blood flow through the parts.

Where the vasoconstrictor influences fail, the arterial sheath becomes relaxed, and the tonus falls. This condition is seen in Addison's disease, where there is a lesion of the adrenals and implication of the chromaffine system. In this condition, adrenalin only will act as a stimulant of the sympathetic system. In the normal blood the adrenalin has a tonic effect on the vessels. In Addison's disease there is diminution of adrenalin production, and a decrease in blood pressure that can be artificially and temporarily increased through injection of the drug.

Statements such as these, in which the literature abounds are not quite in consonance with the views of others. For it is asserted, of late,¹ that the chromophile tissues do not maintain, nor help maintain the normal tone of the blood vessels or other sympathetically innervated structures. Nor is the medulla of the adrenal body essential to life.

The condition described as "war edema" is another instance of generalized insufficiency of the vasomotor system. In this disease the kidneys are intact and there is marked salt retention, bradycardia and diminished blood pressure: a true example of *chronic hypotonia*. Furthermore, in acute fevers, such as epidemic grippé, a sudden failure or insufficiency of the vessels has been noted, particularly as a complication of pneumonia.

Localized Derangements of Vascular Tone.—Diminution of the vascular tonus can be brought about through the action of hot baths; and a compensatory vasoconstriction in other territories is said to occur. There is believed to be a certain antagonism in the bearing of the skin and of the internal organs as far as the vessels are concerned. When there is marked muscular activity, the vessels of the splanchnic territory are said to contract. Transitory increase in tension of the vessels of such territories has been described as giving rise to *vascular crises* (Pal² Hoffman,³ and Fahr⁴).

According to this theory the vessels (abdominal, thoracic, cerebral territories, or in the extremities) may react by contraction to certain stimuli; even Raynaud's disease and intermittent claudication are regarded by some as examples of such effects(?).

¹ Pearlman & Vincent, *Endocrinology*, 3, 1919, p. 121.

² Pal, *Gefässkrisen*, Leipzig, 1905.

³ Hoffman, *Jahresk. z. ärztl. Fortbild.*, 1919, p. 3-18.

⁴ Fahr, *Zentralbl. f. Herz. u. Gefässkr.*, 1918, H. 3, p. 25.

Vascular insufficiency can also be well studied in arteriosclerosis. This disease may affect all of the arteries, or may be localized: arteriosclerosis of the aorta, the coronary artery, vessels of the splanchnic territories, vessels of the kidney, brain and extremities may be given as examples. Therefore, localized disturbances are to be expected in the territories supplied by the affected vessels. The normal regulating mechanism in these territories must be more or less in abeyance.

Peripheral arteriosclerosis can exist with little or no involvement of the vessels elsewhere. The evidences of arterial insufficiency are particularly manifest in the muscle territories. Because of the intensive demands of the working muscles, the arteries cannot allow of adequate supply when certain functional disturbances arise. This is particularly the case in the lower extremities, where so-called intermittent claudication is the clinical expression of these disturbances.

In Raynaud's disease and erythromelalgia, insufficiency or malfunction of the nerve mechanism of the vessels is believed to exist.

CHAPTER X

LOCAL CIRCULATION

A discussion of the pathological local circulation should comprise the alterations due to diminished blood supply (local anemia or ischemia) and to increased blood content (local hyperemia including rubor and erythromelia).

LOCAL ANEMIA OR ISCHEMIA

Causes.—Whenever a given circumscribed part of the body receives less than its normal quantity of blood or almost no blood, we speak of local hypemia (or ischemia, namely diminished blood content) or of local anemia (failing or absent blood content). A part is practically never completely depleted since some blood always remains in the vessels. Custom, however, permits us to extend the appellation anemia even to those states in which the blood depletion is incomplete. Some of the continental physiologists have been wont to make use of the term *local hypemia*, to more accurately designate a state of diminished local circulation.

The author has for years employed the word *ischemia* to designate that condition in which certain obstacles to, or checks upon the normal circulation manifest themselves in a part. One may even in the normal, produce slight local anemia (or relative anemia) through the mere elevation of a part, by virtue of which the venous return is enhanced and the delivery of blood made more difficult.

There are a large number of other coefficients that influence the production of ischemia. Amongst these may be mentioned the following: the mechanical factors of obstructive arterial disease, the effect of drugs (adrenalin), thermal and mechanical forces as well as neurogenic, and even psychic influences. The lumen of an artery may be reduced, or wholly abolished through thrombosis or embolism, or from alterations in the struc-

ture resulting from disease processes (luetic endarteritis, atherosclerosis, thrombo-angiitis, etc.). Local ischemia may also be the sequel of the mere contraction of arteries of supply, or even of capillaries. Such results are attributable to forces acting directly or indirectly through the nervous system. *Adrenalin* may act directly as a vasoconstrictor, as also, *ergotoxin*, the alkaloid that is responsible for the condition of *ergotism*. Cold also contracts the vessels. A varying predisposition to thermic influences finds an illustration in the extreme susceptibility exhibited by the cases of "dead fingers" or *doigt mort* due to moderate degrees of cold. The fingers of such individuals may suddenly become pale, cold and even livid immediately upon immersion in cold water. Here there is an illustration of vasoconstriction through *reflex nerve* paths. Here neurotic phenomena may even cause the skin vessels of one arm to contract when only the other arm is exposed to cold.

In addition to these factors, there are also those motivating agencies that evoke arterial spasm in the presence of a *spasmophilic* tendency. These evince their most exquisite manifestations in Raynaud's disease.

As for the newer theories on the physiology and pathology of the vegetative system, we refer to Chaps. V and VI, in which both the rôle of the calcium salts, the endocrines and the vegetative nervous apparatus have received due consideration.

Local anemia or ischemia may arise through increase of the outflow without corresponding increase of the inflow of blood; through mechanical displacement (compression) and through diminution of arterial influx up to complete cessation of flow (complete ischemia).

We are interested here not so much with the first two of these. The last will be described in further detail, since most of the maladies leading to circulatory derangements of the extremities belong to this type.

Diminished Arterial Influx.—A number of causes for this type of ischemia must be considered: (1) deficient filling of a vascular territory; and (2) defective filling by reason of primary diminution of the size of the afferent vascular lumina.

1. A vascular territory may be poorly supplied (*a*) by reason of abnormality of heart action; (*b*) because of depletion due to the deflection of blood into other territories or organs; and (*c*), defective vascular fulness in non-functionating paralytic parts.

We need not dwell upon these well-known causes, since the student will have received adequate knowledge thereof in his reading along other lines. It may be well to confine the discussion, therefore, to the second type where the afferent vessels are narrowed either mechanically or functionally.

2. *Mechanical Diminution of the Patency of the Arteries.*—The consequences of mechanical closure of a vessel through ligation, compression, embolism, thrombosis or advanced mural changes depend upon the time during which the occlusive process is elaborated and more particularly upon the presence or absence of collateral connections with other arteries. The immediate effects upon the territories supplied, the clinical manifestations and the responses that are evidences of Nature's compensatory processes, are fully described elsewhere.

Neuro-irritative or spastic anemia or ischemia may be produced by local contraction of small vessels. Functional contraction of arteries may take place through direct action such as cold, through chemical influences, or through the nervous system. These various types will also be given due consideration.

The Consequences of Local Ischemia.—The striking visible evidence of impaired and diminished circulation of a part is the change in color or *pallor* (blanching). Careful observation may then demonstrate also a certain degree of diminution in volume of the part. The latter, however, is due in part also to the reduction of quantity of tissue fluids other than the blood. When ischemia continues over a sufficient period, the part becomes *cooler* because of the limitation of amount of blood delivered and altered chemical activity. Functional derangement of the cells, too, results. In short, alterations in *color, volume, temperature* and *function* appear, and they vary according to the degree of circulatory deficiency, its rapidity of onset, its duration, the possibilities of collateral compensation in the affected territory and the susceptibility of the part or organ involved. Naturally the amount of circulatory impairment depends on the degree of obturation of the supplying vessel, and the number of vessels implicated.

So also, the advent of the obstructive factor will, to a degree, determine the issue; a sudden embolic closure being more to be feared than slower obturating processes.

The duration of interference, too, is important in that temporary forms of pressure are relatively insignificant in their effects as compared with lesions due to embolism, thrombosis, or disease of the vessel walls.

The collateral blood supply may be a determining factor. Normally, certain preexisting channels are present, which in the face of obstructing agencies, act as devious surrogates in which an abnormally high blood pressure is produced.

HYPEREMIA

Another result of circulatory derangement is the condition of *arterial hyperemia*. Active hyperemia has been employed to characterize the circulatory condition in an organ in which the blood flow is one of its functions. There may, too, occur hyperemias of *paralytic* nature with lesions of vessel nerves.

For the establishment of hyperemia, dilatation of arteries is a *sine qua non*. In the normal, such change in the lumina takes place by virtue of nerve action, either through stimulation of the vasodilators or diminution in the tonus of the vasoconstrictors, or both. The facial blush is a common example of arterial hyperemia. In particularly susceptible individuals the normal relationship between blushing and the motivating factors is disturbed. So, in addition to the usual exciting moment of shame, minimal irritants such as warmth may suffice to bring it about.

In conditions of neuroparalytic hyperemia with paralysis of the vasoconstrictors, (except after section of the cervical sympathetic), it may be difficult to establish the neurogenic character of arterial hyperemia. Although we know from experimental work that excitation of various centripetal nerves may cause arterial hyperemia, it is very hard to recognize the provocative factors in the human. Investigations have shown that the intensity of the irritant may determine whether constricting or dilating effects are obtained. Stimulation of sensory nerves has been followed by local vasodilatation and constriction in more remote territories.

Increase of the surrounding temperature usually causes dilatation of the cutaneous vessels (a reflex effect).

Many erythemata are of nervous origin, such as symmetrical hyperemic spots (*tâches cérébrales*). In diseases of the spinal ganglia (with herpes), arterial hyperemia may follow excitation of vasodilators. The vasodilator paths are supposed by some to be identical with the centripetal nerves which, therefore, would functionate in an antidromic sense.

As for the substances that are able to exert a direct dilating effect on the vessels, it has not as yet been established whether their action is through peripheral endorgans of the vasodilators or by virtue of a paralytic action on the vessel musculature. These substances, however, show a selective action in that they may cause dilatation of some, constriction of other territories.

The *postanemic hyperemia* following the cessation of compressing forces (tourniquets, Esmarch bandages,) is an example of arterial hyperemia. Its clinical analogy can be produced when we elevate an extremity in which arterial occlusion is present, wait for ischemia to develop and subsequently allow the limb to hang down. A marked *reactionary* or *induced rubor* (*erythromelia*¹) is a characteristic phenomenon. Its intensity is greater than the chronic hyperemia which may or may not already be present in obstructive arterial disease.

Some physiologists attribute the establishment of postanemic hyperemia to reflex nerve action. It is known that such hyperemia may follow section of a nerve. But this does not preclude the local influence of neurogenic impulses; for both anemia and sudden return flow of blood into an area previously excluded from the circulation may bring about local excitation of nerves. As examples of such may be cited the fibrillary contractions of muscles when blood reenters anemic parts. These occur even after section of the motor nerve, but are put in abeyance after curarization. From this it can be concluded that irritation of the motor nerve endings in the muscles is responsible for the phenomenon.

Vasoconstriction and even vasodilatation are usual and common sequences of obstructive anemia or ischemia. Both of these may be of neurogenic origin. Clinically, analogies will be brought to the reader's attention in the discussion of the vasomotor manifestations accompanying hydrostatic (mechanical) phenomena in thrombo-angiitis obliterans. Here we may merely mention that a chronic or more or less permanent hyperemia is one of the characteristic manifestations of the disease. Its origin is probably in part hydrostatic and mechanical, and in part neurogenic. After elevation of the limb in this affection, ischemia is manifested by the blanching of the part; and if the limb be subsequently allowed to hang down, an excessive amount of rubor, quite out of proportion to the degree usually present, is evoked. This corresponds to the above described postanemic hyperemia (induced, reactionary rubor).

Singular and noteworthy examples of neurotic vasomotor constriction can be frequently demonstrated. It was pointed out, above, that both temporary vasoconstriction and more or less prolonged vasodilatation are the neurotic effects of ischemia of the parts. A clinical example may often be observed in thrombo-angiitis obliterans. For if a limb be made to blanch for an adequate period of time in this disease of obstructive vascular nature, and the part be then gradually brought down towards the horizontal or below this level, a gradual blush (hyperemia) will be observed to travel from the periphery in a central direction. Strange to say, however, the *pallor may persist in the horizontal* position for sometime, even though it had been previously proven that a fair degree of color was the rule in this

¹ A term employed by the author and elsewhere described in extenso (Chap. XLVI).

posture. Or islands of color may be of prolonged duration. These two phenomena, although presumably in part of mechanical or hydrostatic nature, can be more readily explained on the assumption that the neurogenic vasoconstriction induced by the anemia is *unduly sustained*, and the reactive vasodilatation (rubor hyperemia) correspondingly delayed.

Venous Hyperemia.—This is essentially the opposite of local ischemia for, whilst the former arises through impediments to the inflow of the blood, the latter is due to defective outflow. As a rule, mechanical causes are at work so that we speak of mechanical or passive venous hyperemia. The large number of collaterals prevents any appreciable interference with the outflow when but one or a few channels are obstructed, except when one of the larger trunks is involved.

Although it is usually believed that the veins themselves play a passive rôle, the possibility of a functional participation of these channels has been suggested by the results of experimentation.

Cardiac insufficiency may cause venous stasis, or when with increased intrapulmonary tension, the outflow through the veins is impeded. In the extremities the insufficiency of the valves of the veins adds to the difficulties of the venous transmission of blood, and in these circumstances, the effects of gravity are felt. Any muscular contraction or cramp may be a further impediment.

The absence of *venous tone* should also be mentioned as another such factor. External (particularly constricting) pressure, thrombosis and endophlebitis have an obstructive action.

The *consequences of venous hyperemia* in a part are: dilatation of visible veins, cyanosis, increased volume of the affected region, and diminished temperature. The cyanosis is not essentially due to the enlargement and engorgement of the visible channels, but rather to the alteration in the color of the blood. This is a sequence of the diminished arterialization and the greater carbon dioxide content that the retarded flow brings about. In contrast to the effect of arterial hyperemia, reduced warmth is often characteristic of stasis.

Venous blood, according to Krogh, never induces any local contraction of capillaries, but often a pronounced dilator action; the latter may, however, be counterbalanced by strong constrictor stimuli that exert their action directly or through sympathetic nerve fibers on the capillaries' contractile cells.

Acrocyanosis.—A dusky discoloration (often spoken of as asphyxia or cyanosis) of the fingers, hands and the feet, may occur in a number of different affections. In some of these the general circulatory conditions are at fault, in others the constitution of the blood; and, in still others there are transitory, sometimes fugitive periods of vasomotor instability.

The Asphyxia of Irritable Hearts.—Abnormal changes of color, such as lividity or pallor, are frequently noted in the extremities of patients suffering from irritable heart (Briscoe). The usual agent inciting color changes is cold. Washing the hands in cold water, or a sudden change of room temperature, conditions that would ordinarily not affect normal individuals, seem to call forth the peripheral asphyxia.

There are cases too, in which the hands are said to be livid, cold and numb at all times, the discoloration involving the fingers, the hands, and even the wrists, with often a bluish tinge over the forearm. The compression or expression test¹ produces a dead white patch that evidences the sluggish-

¹ Described on page 163, as a rough index of circulatory activity; but it is dependent on vasomotor influences.

ness of the circulation, for the color is but slowly regained. The color of the blood, too, when allowed to ooze out through a pin prick, is very dark, so that we have here three essential features suggestive of retarded capillary circulation and venous stasis; namely, coldness, darkness of the blood, and sluggish return. The mucous membranes are not cyanotic.

From experiments on capillary pressure in reflex response to cold, Briscoe¹ concludes that the immediate reaction to cold is a transient fall in capillary pressure probably due to a constriction of the arterioles. For this would diminish the supply of the blood to the capillaries and reduce the pressure. But a simultaneous contraction of the venules would compensate and bring the capillary pressure up to normal again, in spite of the diminished flow through the extremities. That reaction to cold may be of remote nature has already been mentioned. When one hand is placed in cold water, it has been demonstrated that the flow of blood through the other hand is cut down to nearly one-half (Stewart² and Hewlett³). An increase in irritability of the vasomotor system, as is known to exist in Raynaud's disease, was also brought to light through the studies of Stewart, when in his experiment of immersion of one hand in cold water in a case of Raynaud's disease, the flow in the other hand was instantly reduced.

In acroasphyxia attending cardiac irritability, the capillary pressure rises above the normal, while in controls it does not quite return to normal. From this it has been concluded that there is a vascular spasm distal to the capillaries, namely, in the venules. With sufficiently long continued spasm the velocity of the blood stream is diminished and the blood becomes venous.

The pinkish areas in cases of blue hands have been explained on the theory that the mechanical alterations in the blood, due to increased carbon dioxide and other metabolic products may bring about dilatation of arterial capillaries by direct chemical action.⁴

CHAPTER XI

FUNCTIONAL DISTURBANCES OF PERIPHERAL CIRCULATION

These may be divided according to their main functions into derangements due to altered or inadequate blood circulation and into abnormalities of the fluid exchange through the capillary walls. These two are in intimate relationship; indeed, the latter being in a measure dependent on the former.

1. Derangement of the Capillary Flow.—Variations in rapidity of capillary flow are observable in different territories. A distinction can be made between the capillaries, the precapillary arteries and postcapillary veins.

Increased blood pressure can intensify the flow in the capillaries when these are not narrowed. In hypertonic conditions (nephrosclerosis) the capillary flow has been found accelerated; so also in aortic insufficiency. Where the capillaries are narrow as in marked arteriosclerosis, retardation occurs. A slow flow has been noted in acrocyanosis, in Raynaud's disease,⁵

¹ Briscoe, *Heart*, V. 7, 4, 1920, p. 43.

² Stewart, *Heart*, 1911-12, III, 76.

³ Hewlett, *Arch. Int. Med.*, 1911, VIII, 591.

⁴ See Chaps. XI, XIII, LXXXVII.

⁵ For the latest views on Capillary Microscopy in this disease see Chaps. CVI et seq.

erythromelalgia, scleroderma, and the passive hyperemias of cardiac or vascular origin. In general we may say that increased pressure in an artery of supply due to narrowing of the latter, causes retardation of the capillary stream.

The changes in capillary flow result in corresponding alterations in capillary blood pressure. This endocapillary pressure is increased both in active as well as in passive hyperemia, whilst it is diminished in ischemic conditions. With too great a diminution of endocapillary tension the nutrition of the part must suffer; some injury, too, ensues upon too intensive an increase of pressure.

As a consequence of a rise in endocapillary tension, diapedesis of the red blood cells is a common occurrence, particularly with passive, but also with active hyperemia. The character of the capillary wall, however, also plays a rôle in this filtration. A predisposition or hyperpermeability may be acquired by the capillaries through the induction of artificial ischemia (post-anemic diapedesis). A predisposing factor, therefore, is artificial ischemia, which may be observed after the use of an Esmarch bandage. Old people are especially susceptible. Diseases, too, that alter the constitution of the vessels (scarlet, grippe, etc.) may also increase the susceptibility to diapedesis.

These observations are of some clinical importance in that they teach the lesson that the production of too intensive ischemia through whatever means should be avoided whenever marked obstructive disease of the arteries of an extremity is at hand. The application of an Esmarch or Martin bandage for purposes of making functional tests is not without danger, for irrespective of the perils of thrombotic sequels, the extravasation of red blood cells may predispose to local necroses and gangrene. So, too, the application of the author's *postural treatment*¹ for enhancing the circulation and nutrition of the part, must be so carried out that the period of induced blanching is minimal.

Through the same action a migration of leucocytes, too, may take place (leucodiapedesis). Because of the spontaneous activity of these cells, we usually substitute the word *emigration* for diapedesis. With retardation of flow the white cells approach and are heaped against the vessel wall. Their transmigration goes on, both through filtration and their own motility.

Arterial spasm, when it involves larger vessels as in *Traumatic Angio-spasm*, gives clinical pictures quite different from those following contraction of the *arterioles*. When the latter contract strongly, the blood still seeks the veins through the force of the *vis a tergo*, the capillaries becoming emptied. With this the part blanches and its volume may become lessened. As the veins fill and the pressure therein overbalances that in the capillaries, the part may become cyanotic, and even regurgitation of venous blood may take place. This condition becomes accentuated when the affected part is in a dependent position.

If we test for return of color after digital expression (compression test) in asphyctic skin in which the arterioles are constricted and the capillary circulation poor or nil, the reappearance of cyanotic color must not be mistaken for evidence of circulation, for it is but the venous blood coming into view.

Spasm of venules is said to be possible, but without arteriolar contraction the immediate blanching is absent. Lividity is produced through stagnation of the blood in the capillaries. A generalized spasm of arterioles and

¹ See treatment of arteriosclerotic vascular disease and thrombo-angiitis.

venules is said to occur, and this is followed by ischemia of the part (anemia). Associated is a reduction in volume of the part.

2. Disturbances Due to Impaired Exchange of Fluids.—As far as we know, the capillary walls have partial permeability, not allowing all substances to pass equally well from both sides. The chemical bodies of the absorption stream (from the blood into the tissues) are also different from those of the excretion or outflowing stream (from the tissues into the blood). These functional elective powers disappear as the tissues lose their vitality. For all the phenomena are not explicable on the basis of filtration, diffusion and osmosis, but a capillary secretory activity may play a rôle. The locality of the interchange is probably the intercellular spaces. Alterations in the fluid stream may be of quantitative and qualitative nature.

The changes in capillary pressure also modify the fluid exchange. If we accept the theory that diapedesis may be a sequence of the above, we must also be ready to believe that analogous alterations in the fluid waves may ensue. Indeed, in the occurrence of postanemic edema, we have an example. After artificial hyperemia, an intensified lymph current has been noted as an accompaniment of the increased absorption stream. A diminished capillary pressure can evoke an increase in the excretory or outflowing stream.

An excess of capillary pressure may cause fluids to percolate outwards from these channels; and the increased intercapillary tension may follow local arteriolar dilatation, venular contraction or venous obstruction, *edema* resulting from obstruction to venous flow. It is not certain as to what rôle forces other than mere filtration, play in this abnormal fluid exchange. The theories set forth are that the sluggishness of the capillary flow increases the permeability of the capillary walls; or, that certain alterations in the metabolism of the tissues outside of the capillaries make for increased fluid imbibition from the blood.

For an understanding of some of the trophedemas and conditions of neurotrophic nature that are dependent on deranged capillary function, it may be well to point out that although intracapillary pressure is often responsible for pathologic phenomena in the tissue currents, the *condition of the capillaries* themselves may be the more important. So we have on the one hand, the nutritive disturbances of the capillaries due to anemia and passive hyperemia; but, on the other hand, the alterations that certain substances may produce. Many bodies may increase the activity of the absorption stream. Some are specifically vessel poisons such as the toxin of diphtheria, tuberculin, pneumococcus serum, etc. But even for the action of these substances a certain predisposition or idiosyncrasy is necessary. (This is seen in the abnormal susceptibility of certain individuals to strawberries and shell food.)

Some authors believe that the tissue stream may be modified through nerve influences. These may be manifested in the production of a neurotic hyperemia as well as in an altered permeability of the capillaries. The urticaria following mechanical irritation of the skin is an evidence in favor of such a function. Whether a preceding or coexisting reflexly evoked hyperemia is responsible wholly or in part, is still a mooted question. In the *evanescent edemas* without hyperemia, a direct neurogenic basis is probably present.

The administration of calcium chloride tends to reduce the permeability of the capillaries and is therefore of value in circumscribed edemas. Increased density of the cellular membrane through increase of calcium content as well as the opposite effect on intensified permeability in the deficiency of calcium salts, are well known biochemical and physiological observations.

To digress for a moment, it may be well to call attention to the theories of some of the more recent investigators on the vegetative system regarding the rôle of the calcium salts in *spasmophilic* tendency. According to these, defective calcium metabolism with diminution of this salt, may be an important factor in the production of hyperirritability of the vasoconstrictor centers.

Functional Derangement of the Lymphatic System.—Although it is known that the intercellular spaces communicate with the lymphatics, it is still doubtful as to whether they are separated by a thin membrane or not. Tissue juices or fluids must not be confused with lymph. All cells are not in direct communication with the lymphatics through the tissue fluids, since some cells are directly apposed upon the blood capillaries.

Here, too, quantitative and qualitative changes in function occur. Abnormal acceleration or retardation of the lymphatic flow represents the former. These may be the result of variations in the production of lymph and in its outward flow.

Mechanical factors, such as pressure, tumor growth, collections of fluid and thrombosis may diminish the outflow of lymph. Diseases of the lymphatics and lymph nodes may interfere with the lymph flow. When there is increased pressure in the venous system, the discharge of lymph into the veins may be impaired.

Cessation or diminution of lymph flow may set in when the production of lymph is correspondingly defective as in arterial ischemia. There are a number of substances that increase the lymph flow. Amongst these are hypertonic salt and sugar solutions injected into the veins.

Disturbances of the Lymphatic Stream of Capillary Origin.—Since derangements of flow in the capillaries are transferred to the lymph stream, accumulations of fluid in certain parts of the body may result. Collections in the tissue spaces are known as edema.

When a large venous trunk of an extremity is ligated in an animal, there usually follows an increased lymph flow without any edema. If we simultaneously interfere with the lymphatic flow, or if the blood be hydremic and the vasoconstrictors paralyzed, then edema may ensue. In general venous stasis, however, edema appears since by reason of the increased venous pressure the lymphatic outflow from the thoracic duct into the subclavian vein is impeded.

Edema usually follows derangement of the capillary walls. It can, however, result from alterations in the cells by virtue of which these give off larger amounts of fluid. As corollaries, we may mention that transudates seem to indicate an origin through capillary lesion, whilst the edemas, because of their salt content, may be more correctly explained on the basis of disturbances in the cell function.

Local *fugitive edemas* (edema fugax) warrant the supposition that both a local predisposition of the capillaries as well as neurogenic factors or blood composition, may be at fault.

Inflammatory edema has several causes including lesions of the capillaries and tissues.

Disturbances in Continuity of the Vessel Constituents.—Pathologists (Hering) speak of solution of continuity in respect to the cells of a vessel and a more gross variety in which the cells themselves are broken up. Whilst the latter may occur in any vessel, the former applies only to the capillaries in which varying degrees of separation of the cells from each other may take place. Solutions of continuity may be produced by a large number of causes. Mechanical or external agencies, increased pressure from within, degenerative processes (atherosclerosis, arrosion) infection with suppuration and necrosis, neoplasms and ferment action—all these are amongst the agencies observable.

In vicarious menstruation, hemorrhages have been attributed to the action of the internal secretion of the ovaries as also to neurogenic factors.

Diapedesis (or the escape of the red blood cells through separated endothelial elements) may be altogether due to increased endocapillary pressure into a certain predisposition of the vessels themselves. The hyperemias are the exerting moments. In the anemias, the factor of susceptibility may be extraordinarily prominent (so also in hemophilias, purpura,

etc.). Various poisons alter the fragility of the vessels. We can gain a rough clinical idea of the degree of individual susceptibility to diapedesis by comparing the tendency to hemorrhages after artificial stasis over a given period with the normal. The usual disposition has been characterized as the "*endothelial symptom*."

THE SUPERFICIAL CIRCULATION IN OBSTRUCTIVE VASCULAR DISEASES

If we were to enumerate the agents through which objectively visible alterations in the superficial circulation are modified, we would include:

- (1) The diminished force of the stream (*vis à tergo*).
- (2) The hydrostatic and gravity forces.
- (3) The changes in the vasomotor mechanism.
- (4) The local forces, that directly influence the autonomic capillary activities.

These all should be taken into account in explanation of the phenomena of asphyxia¹ and rubor,² so often characteristic signs of the obstructive arterial diseases of the extremities.

1. The Diminished Circulation.—To go into a detailed discussion of the altered dynamics that are entailed through the exclusion of existing and important vascular channels, would be a work of supererogation. For, on the one hand, the thesis requires neither emphasis nor explanation for comprehension; and on the other hand, an exact measure of the diminution of volume and celerity of the blood stream is beyond the pale of our applied physiological and clinical methods. We must be content, then, to assume the existence of impaired flow, for, we have no accurate means of estimating the degree of circulatory impoverishment in a given case, beyond that knowledge which the rough clinical methods to be described may furnish us.³ Certain it is, that a sufficient reduction of this flow is often obvious in those significant pallid feet and legs that are cold and blanched even in the horizontal position. That a reduction in the fullness, or even a collapse of arterioles and capillaries of peripheral skin and subcutaneous vessels must obtain through this mechanical cause alone, may be accepted without hesitation. We have elsewhere called attention to the vasoconstriction occurring in arterioles and capillaries as a secondary response.

2. The Forces of Hydrostatic Nature and the Rôle of Gravity may require but passing mention, since their more detailed workings and manifestations will receive attention in other chapters. Through the unnatural imbalance between the strength of the pumping mechanism and the increased local resistance through the exclusion of larger avenues, and the prominence of devious and smaller pathways, conditions are given for an enhancement of the effects of gravity and hydrostatic forces. Indeed, the latter are influential, inversely with the patency of the natural vascular lumina; or *they modify the objective circulatory phenomena more and more, the greater the obturation in the affected vascular territory.*

Whereas the normal limb when elevated above the horizontal, presents a pinkish integument even over the most peripheral parts, gravity and hydrostatic pressure may make for complete blanching when larger vessels are occluded. And so, the position of the part must be taken into due consider-

¹ Vide, Chap. XLVII, Cyanosis in Thrombo-angiitis.

² Vide, Chap. XLVI, Erythromelia.

³ Except perhaps the method of Stewart (Chap. VI) which has not been extensively used.

ation when the fullness of arterioles, capillaries or venules is being investigated or discussed. Whilst elevation may deplete the venules (when the veins are adequate for return), depression may make for stasis and asphyxia when the propulsive forces are inadequate to force the blood through arterioles, capillaries and venules with sufficient celerity.

3. The Changes in the Vasomotor Mechanism.—Many of the basic facts that physiologic researches have brought to light have already been summarized in the chapter on anatomy and physiology of the vasomotor paths. Here we wish to allude merely to those special circumstances in local disease that bring about alterations in the normal mechanism. Such occur both in the neurogenic and organic obstructive vascular affections. Concerning the former, a more detailed discussion will be relegated to the chapters that are concerned with the special classes of vasomotor neurosis. The deviations of nerve function in the latter, however, may properly be referred to here.

Nerve malfunction may result from the following causes.

1. Organic intrinsic lesions of the vessels and perivascular tissues implicating the terminal nerve distribution.
2. Perivascular inflammatory and secondary fibrotic processes (thrombo-angiitis obliterans) influencing the adjacent nerves.
3. Reflex alterations.
4. Exhaustive states.
5. Altered local metabolism and abnormal chemical products in the tissues.

In thrombo-angiitis obliterans the perivascular fibrosis and the inflammatory products of the acute stage may exert an influence on the surrounding sensory and motor nerves. Through the former, both pain impulses and reflexes with vasomotor responses may travel. That pain alone may evoke neurovascular phenomena has been elsewhere mentioned.

We need only emphasize here the great importance of reflexes on the vasomotor functions, for these have been already described. In addition to the multitude of impulses that are constantly received from within and throughout the body, local changes, metabolic, nutritional and pathologic (especially trophic ulcers, etc.) as also external causes (thermal and mechanical) may play a rôle in engendering abnormalities of vasomotor function.

4. Exhaustion.—To what extent an exhaustion of the vasomotor impulses of constrictor type can be produced through overactivity, cannot be accurately determined. That a recoil into a paralytic state or a passive vasodilatation is possible after continued angiospasm, cannot be denied. Investigators have shown that certain chemicals may initiate a condition of constriction that yields to a palsy with chronic dilatation. So, too, may nervous mechanism finally fail, be it through continued and over-excitability or be it through reflexes evoked through intense and constant pain.

5. Chemical Action.—If we base our conclusions upon the data furnished by physiologists regarding the effects of chemical alterations in the tissues on arterioles and capillaries, and the observations of clinicians, we must assume that an abnormal vasomotor mechanism can be induced when pathological nutritional conditions obtain. In this way a reversal of a normal vasodilating response into an abnormal vasoconstricting reaction may occur whenever an unusual stress (exercise) develops an inordinate amount of poisonous constituents in poorly nourished tissues. It has been assumed that the symp-

toms of intermittent claudication (page 156) may be brought about in this way.

In arteriosclerosis and thrombo-angiitis obliterans, where circulation is inadequate, exercise produces an accumulation of CO₂ and lactic acid and a deficiency of O. These chemicals are believed to be able to cause a reversal of the vasodilating into vasoconstricting reflexes. The cramp-like pains that succeed, have been interpreted as the subjective manifestations of this altered physiology.¹ According to Hopkins the normal cycle of events in muscular activity consists of two phases separated in time: the first anaerobic during which lactic acid is formed; the second aerobic during which it is removed. Only with conditions of inadequate oxygenation will this acid accumulate. Perhaps it is this chemical that calls forth the reflex.

CHAPTER XII

COLLATERAL CIRCULATION

By the term *collateral hyperemia* we may designate that arterial flow which occurs in the territory adjoining one whose main artery has become occluded. The origin of such hyperemia depends upon the nature of the arterial distribution. Whenever adequate arterial anastomoses are present, as in the case of the arteries of the hand or the foot, obturation of one large trunk is immediately followed by deflection of the current into other adequate paths. If the arterial connections, however, are insufficient, an anemic focus surrounded by a peripheral zone of collateral hyperemia develops.

The term collateral hyperemia has also been defined as that increased influx of blood which may occur into one of a pair of important sister organs, such as the kidneys, when the artery of one is occluded or the organ itself has been removed. Certain conclusions concerning the physiologic hyperemia occurring in such organs may be extended to the peripheral vascular system. Increased blood pressure consequent upon the occlusion of a large vessel leading to such an organ would not account for the vicarious hypertrophy of the remaining organ; and a reflex irritation of vasodilator nerves has been suggested as a more plausible explanation.²

Another similar manifestation is the secondary or postanemic hyperemia that occurs after transitory arrest of the circulation in an extremity.

Collateral hyperemia is the prelude to, or preliminary stage of an elaboration of a new collateral arterial circulation after occlusion of an important arterial trunk. Its development takes considerable time. Whenever a large artery is ligated, collateral flow occurs in reverse direction and usually with great rapidity. The development of such a current is proportionate to the dilatability of the arteries. In the development of collateral circulation, either small arterial anastomoses participate or new ones must be formed. As a rule, the anastomosis formation is well marked in a few days.

In collateral circulation, as well as in that of collateral hyperemia, the mechanical factor of increased pressure does not sufficiently explain its origin. Continuous dilatation of the arteries presupposes *diminution* of the tonus to nerve influence; and we would suppose an *increased* tonus after increased pressure. The genesis of collateral hyperemia after closure of a large arterial trunk, therefore, must be regarded rather in the light of a product of altered innervation, possibly of irritation of the vasodilators. *Pari passu* with the dilatation of the small vessels, increased growth takes place, so that large thick walled vessels may result from small thin ones.

¹ Hopkins, Harvey Lectures, 1920-1921, p. 210.

² See Chapter XLVI on Erythromelia and the explanation of rubor.

The *collateral avenues* are preexisting channels whose total capacity bears a relationship to their size (caliber), number, patency and dilatability. Anything which interferes with the accommodative enlargement of these, such as sclerosis and congenital hypoplasia, may correspondingly limit their functional value under special stress. The local increase of pressure above the point of arterial obstruction is important in the development of the collaterals. Its degree is proportionate to the size of the closed vessel, and also influenced by the general blood pressure. How delicate the mechanism causing circulatory disturbances is, may be concluded from the observation that hypertension may be produced also through reflex causes as well as mechanical. It is even believed that the chemical alterations in the anemic territory may bring about a rise in tension. So also, dilatation of the collaterals may be evoked by reflex as well as mechanical forces. Since the general pressure depends on the heart action, the development of collaterals, too, will be similarly modified. Weeks and months may be required before the ultimate collateral circulation has been formed.

Bolognesi¹ performed experiments to determine the effect of ligating the external iliac artery in dogs. The ligation was done with a double catgut ligature under perfect asepsis and by the extraperitoneal route. For the first two days following the ligation the femoral pulsations disappeared but soon thereafter returned to normal. The animals were killed after varying periods of time and the vascular systems of both limbs studied with the X-ray after the vessels had been injected. The results of this study are summarized as follows:

(1) The arteries below the ligation were found to be enlarged and to possess more numerous secondary branches than those of the corresponding area on the normal side.

(2) There was no return of circulation in the tract of the external iliac artery at the end of one month but after two or three months a true collateral circulation had been established which was represented either by communicating arterial branches or by complete restoration of the segment of the main artery which had been excluded between the two ligatures.

(3) The gluteal branches of the iliac artery, and especially these of the inferior or ischiatic gluteal artery, took part in the formation of the collateral circulation becoming larger and richer in branches. These branches anastomosed fully with the femoral branches.

The results verify the theory as to the establishment of collateral circulation which was brought forward by Porta as far back as 1845. They demonstrate also that the increase in size of the preexisting collateral arteries is of greater importance than a very great increase of newly-formed vessels. This vascular dilation persists until the collateral circulation established is sufficient.

It has often been pointed out that a congenital hypoplasia of the vascular system (sometimes cardiovascular) may be one of the predisposing factors that render certain individuals, possibly also certain races, susceptible to vascular affections. Indeed, for some of the vasomotor groups this theory has found adherents. So also, the hypothesis has been extended to the cases of organic vascular disease.

Whether or not a congenital maldevelopment, implicating, therefore, possible collaterals as well, is influential in preventing the proper and adequate compensatory enlargement and dilatation of surrogate circulatory paths, is a question worthy of consideration. If vessels are inherently too small, it is not unwarranted to assume that when obliteration of important avenues of circulation interrupts the blood flow, the collaterals will become insufficiently developed and that gangrene may eventually ensue.

From the anastomotic by-paths already existing, certain laws can be deduced as to the means of ascertaining the efficiency of the collateral circulation. If we study the course of these anastomoses and that of the palpable portions of the femoral and popliteal, we will learn that isolated compression of either vessel might give reliable information as to the circuit through which

¹ Bolognesi, G., *Chir. a organi di movimenta*, 1919, III, 403.

the collateral circulation travels. If, for example, we arrest the femoral artery at Poupart's ligament, after having induced ischemia in the limb, either through an elastic bandage or prolonged elevation, and the circulation returns to the blanched parts in the pendent or horizontal position, we are warranted in concluding that a new source of blood supply has been established from a higher level. Such extensive central displacement of the point of influx is of rare occurrence.

If the femoral and popliteal are patent and the latter is similarly tested, a positive flush or reestablished circulation would denote, too, that the collaterals are adequate, arising above the level compressed. The anastomotic paths could emanate then from any level between that tested and the femoral test point above.

On the other hand, should color fail to return, the totality of arterial supply must be derived at and below the point at which the circulation was artificially arrested.

Unfortunately, the femoral artery is not easily accessible to extraneous obliteration by compression except in its upper part, so that more accurate findings of the collateral niveau cannot be easily ascertained. Enough data, however, can be put at our disposal to warrant interesting deductions.

If the test fails (circulation does not return after compression) at the popliteal level, certain prognostic inferences may be made, to wit, that a sudden thrombosis of this region would leave the distal parts without efficient by-paths. Conversely, those patients in whom the result is positive (circulatory return) would offer a better immediate prognosis.

With a positive test at the popliteal and a negative one at the common femoral, the intervening artery, in its totality, offers possibilities for ascending blockage that must be compensated for by the remaining patent and central portion of its course.

Demonstration of Collaterals in Obstructive Vascular Disease.—Some indications, as to the existence of effective new vascular by-paths can be obtained by compression of the femoral artery in the case of the lower extremities. Whenever chronic rubor is present, compression of the femoral artery for from 2 to 5 minutes may not suffice to efface the color of the foot in the diseased extremity, whilst similar compression on the healthy side produces marked blanching (*paradoxical ischemia* on the healthy, *paradoxical rubor* on the diseased side). This would indicate that new interanastomoses, connecting points above and below the femoral artery, are more efficient in the diseased than in the healthy limb.¹

The Course of New Channels.—The usual concept of these vascular by-paths is vague. All will concede their teleological significance—that they act as surrogates, devious, but nevertheless, purposeful avenues; and that through interanastomoses they succeed in delivering a sufficiency of blood even when large arteries are occluded. Little is known, however, as to the exact course along which the blood flows in any given case; whether the circulatory stream is shunted back again into an important vessel and thence to the periphery, whether altogether new routes are followed, or whether a combination of both exists.

Perhaps it is not generally appreciated that, when ligation of an important artery is undertaken, the blood tends to seek and enter the main channels again at some point beyond the occlusion. According to recent observations the task of the collateral is mainly to reestablish communi-

¹ See also tests for abnormal vasomotor reactions in thrombo-angiitis, Chap. LIV.

cation with the continuation of the main artery, and not to form a new arterial system of more extended course.

When we speak of the collateral circulation in pathological conditions, we must visualize for ourselves the three factors upon which the new course of the circulation depends. These are: firstly, the situation of the most proximal point of obturation in the main vessel; secondly, the condition of the vessels beyond the central point of blockage—as to whether they are patent, narrowed (atherosclerosis, arteritis) or occluded (thrombo-angiitis obliterans); thirdly, whether the sudden advent of a centrally situated obstacle (obturation, ligation, thrombus, compression) is immediately or remotely followed by secondary stagnation, or accretion thrombosis in the arterial or venous channels.

The problem of even vaguely appraising the direction of the collateral paths through existing anastomotic channels becomes difficult *pari passu* with the amount of impairment of the integrity of the arterial tree beyond the point of occlusion. Whilst it is easy to judge approximately as to the new current when a large artery is ligated, or when a small embolus is lodged and unaccompanied by secondary thrombosis in arteries that are healthy and patent, a very perplexing and intricate condition obtains when we are ignorant of the exact extent of a preexisting occlusion in the peripheral arteries. Therefore, in arteriosclerotic obturation and occlusion and in thrombo-angiitis obliterans, the sudden advent of thrombosis or embolism in larger more centrally located trunks offers a more dubious outcome, necessitates a more devious and circuitous route for the substituting arterial paths, and may make reestablishment with the former currents impossible.

The Collaterals When the Peripheral Arteries are Patent.—The frequently accepted assumption that the ends of the extremities are in more imminent danger of gangrene, the nearer to the trunk the ligature is placed, is not in consonance with experience. And so it has been observed that one can tie off the axillary artery and the common femoral without much risk. Often the ligation of the femoral below the profunda is dangerous, while ligation of the popliteal artery is almost always followed by gangrene.

In some investigations (Hotz) it was found that adequate collateral paths are in evidence, wherever large muscle masses require supply, and that at the insertions of muscles in the regions where transition into tendons occurs, there is but a sparse distribution of the arterial by-paths.

In an attempt to explain two striking clinical observations on the frequency of gangrene after ligation at certain levels in the course of the main arteries of the lower extremities, some authors have concluded that the multitudinous smaller muscular branches are perhaps even more important than the larger and discrete anastomotic channels nourishing tendons, fascia and bone. The lack of development of muscular branches is given in explanation of the occurrence of gangrene, when the popliteal artery is ligated. The anastomotic channels about the knee (see Fig. 31), although apparently sufficiently large, do not seem to suffice when sudden occlusion of the popliteal artery occurs. On the other hand, when a process of slow development (such as tumor or aneurysm) has gradually diminished circulation in this region, the collateral paths may have become adequately enlarged. In these circumstances they are able to cope with the sudden emergency that arises when complete occlusion by thrombosis or ligation eventually occurs.

The *arteria profunda femoris* has been considered important, for through its anastomoses with the pelvic gluteal and sciatic arteries, it may act to reestablish the current below its site of origin, when occlusion of the common

femoral takes place. This explains the paradox that sudden obturation below the profunda may be even more dangerous than arrest of the circulation above its point of origin.

A reference to Fig. 31 will recall the anastomoses about the knee joint known as the circumpatellar anastomosis or *rete patellae*. In this rich network are engaged vessels in the superficial fascia surrounding the patella, with branches to the patella, the knee-joint, capsule and neighboring muscles. The vessels partaking in its formation comprise: from above (1) the anastomotica magna from the femoral and the descending branch of the external circumflex; laterally, the internal (3) and external (2) superior, and the internal and external (5) inferior articular branches of the popliteal, and the muscular branches of

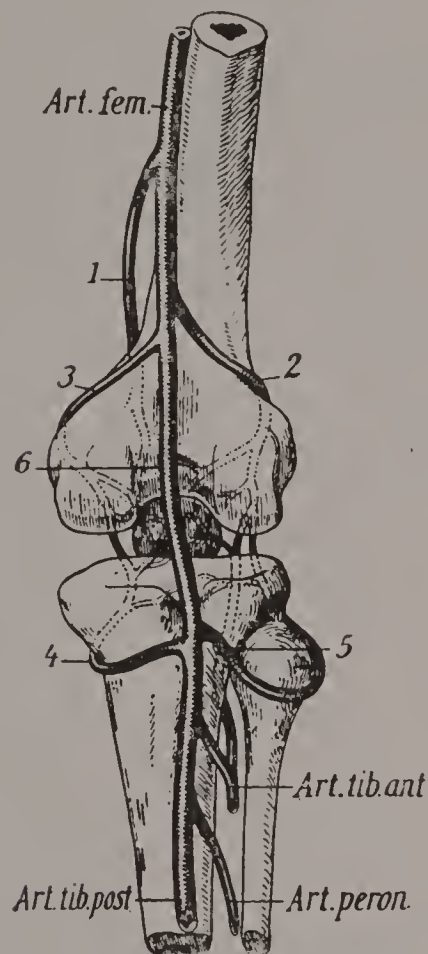


FIG. 31.—Schematic rough drawing of collateral paths about the region of the knee. (Hotz)

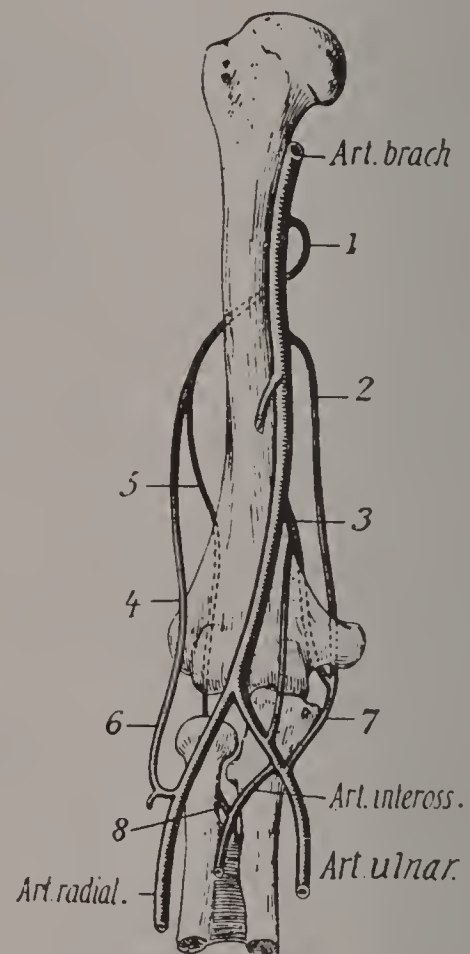


FIG. 32.—Schematic rough drawing of collateral paths about the region of the elbow. (Hotz)

the same artery; and from below, the anterior tibial recurrent. Although these vessels would apparently suffice as anastomotic channels, according to Hotz none of these give adequate supply to muscles. Merely the fascial planes, the tendinous insertions of the thigh muscles below, and the points of origin of the calf muscles above, are supplied with the tendons and capsules of the joints. These circumstances have been regarded as providing an explanation for the danger of necrosis after ligation of the popliteal artery.

In the case of the elbow (Fig. 32) similar conditions obtain. The superior profunda (1) by a medial collateral branch (5) anastomosing with the posterior ulnar recurrent and with the interosseous recurrent (7); and in front of the elbow establishing communication (4) with the radial recurrent (6); furthermore, the inferior profunda (2) or A. collateralis ulnaris superior, also anastomosing with the posterior ulnar recurrent (7) behind the internal condyle, while the anastomotica magna (3) makes connections in front of the internal condyle with the anterior ulnar recurrent; and posteriorly with the posterior ulnar and posterior interosseous recurrent. In view of the fact that these vessels not only supply the capsule of the joint and the tendons (as in the case of the knee) but take care of the circulation of large volumes of muscle, the contention of Hotz seems to be supported in the observation that ligation of the brachial at the elbow may usually be carried out, without danger of gangrene.

In the case of the shoulder region and upper arm, the paradox has been again pointed out that ligation above the circumflex arteries (anterior and posterior or their common trunk) is less dangerous than below that point. A reference to Fig. 33 clearly shows how, by anastomoses of the anterior circumflex with the acromial thoracic with the posterior circumflex and through the anastomoses of the posterior circumflex with the same arteries and the superior profunda (see 6 and 8 in Fig. 33), blood can be directly delivered from the

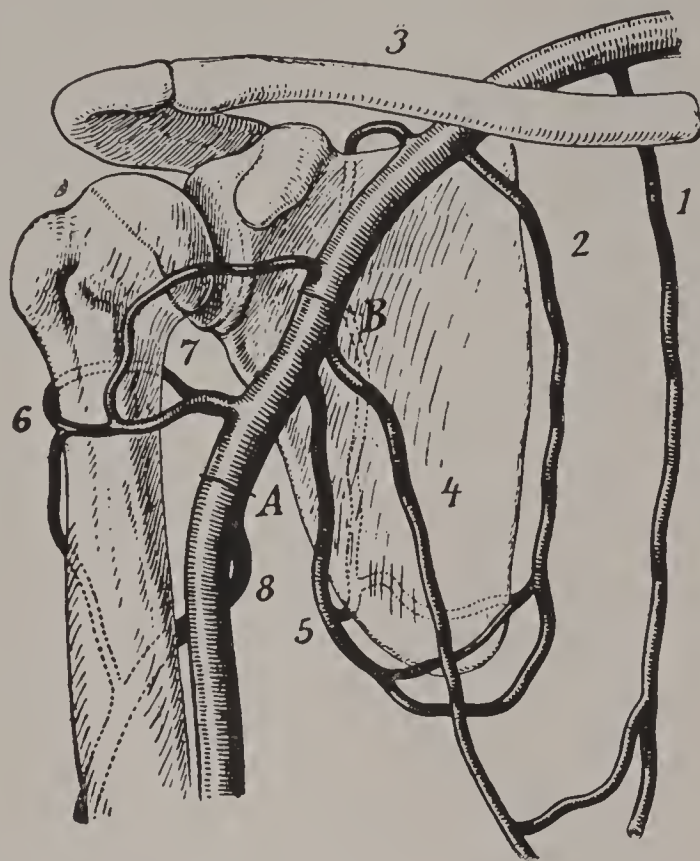


FIG. 33.—Schematic rough drawing of collateral paths about the region of the shoulder. (Hotz)

axillary and subclavian through these channels, through which it may find its way again into the main artery below the point of ligation. When ligation takes place below the circumflex, a more devious route has to be taken by the current. Indeed, ligation below the origin of the profunda should be still more dangerous. Ligation high in the axillary may be borne by reason of the presence of the large vessels, the mammary, subscapularis, and long thoracic.

Therapeutic Development of Collaterals.—Methods for enhancing the circulation must necessarily include those that further the development of collateral channels. Intermittent compression of the femoral or brachial artery has been suggested, and is a procedure that may be of some value in the treatment of obstructive arterial diseases of the extremities.

CHAPTER XIII

CIRCULATION IN THE EXTREMITIES UNDER PATHOLOGICAL CONDITIONS

CLINICAL MANIFESTATIONS

There is no better teacher of the varied circulatory phenomena resulting from pathological conditions of the vessels of the extremities, than the clinical manifestations that shall hereafter be described. Careful observation and comparative appraisal of the normal and abnormal clinical manifestations

are most illuminating. Through these we will more clearly appreciate the circulatory phenomena in diseases of various types and causation, than through theoretical and physiological considerations alone. Nevertheless, it may not be amiss here to dwell briefly on the more abstract questions, leaving their amplification, explanation and illustration for subsequent chapters.

The interpretation of the phenomena of disturbed circulation meets with an abundance of pitfalls, if we do not carefully weigh the various factors that may enter into the resultant subjective and objective states. Although the blood supply of the extremities, and especially of their more remote portions, depends primarily on the size and patency of the arteries and veins, many other elements, both general and local may act to modify the abundance and rapidity of the flow of blood. We need hardly dwell upon the importance of the cardiac factor and general systemic condition, but shall confine ourselves to the agencies of more local source and effect.

For example, a maldevelopment or *hypoplasia* of the peripheral vascular tree is a condition common enough to warrant serious consideration, both because peripheral nutrition suffers then more readily when vascular disease is at hand, and also because of its vitiating action on the development of adequate collateral channels. The presence of such an inherent anatomical mediocrity or inferiority must be deemed possible in any given case, and its participations carefully weighed in every instance of failing local circulatory compensation. Just as aplasia and anomaly must be constantly kept in mind when the clinician makes a critical appraisal of any given case of surgical renal lesion, so here too, one must not lose sight of the factor of congenital hypoplasia.

The multitudinous distribution of the vessels, their variation in capacity, their subserviency to alterations both of organic, functional and neurotic nature, allow of kaleidoscopic combinations of manifestations.

The effects of obstructive lesions will be distributed, in a measure, over the area supplied by the vessel or vessels involved. But only with this reservation, to wit: that these effects are limited in intensity and in extent by time and the possibility of substitutions through other circulatory avenues. So, whilst the quantity of blood and rapidity of flow may be objectively and subjectively manifested in certain areas of the normal distribution at a time immediately following the advent of a sudden arterial obstruction, the intervention of preexisting and later of compensatory collaterals, is responsible for partial or complete disappearance of all phenomena.

Serious alterations (in the vessel integrity) may have as their consequence, no appreciable manifestation other than those of diminished blood supply, decreased warmth and slight sensory disturbances. But where a large territory is affected, by virtue of the exclusion of more central, more important and larger arteries, or through a larger number of arteries, *associated effects* may be then evoked. These are:

(1) Immediate effects; or the residual changes persisting after rehabilitation of the circulation.

(2) The induced or reactionary processes in the peripheral capillaries and arterioles, viz. rubor, hyperemia, or erythromelia.

(3) The tendency to trophic derangements.

(4) The production of either transitory or permanent lability of the local vasomotor mechanism.

Whereas both subjective and objective signs of a suddenly interrupted or seriously disordered circulation in a given territory are usually definite and

vivid enough to be both experienced by the affected person and easily recognized by the physician, *the slower and more gradual obstructive lesions of the vessels may be easily overlooked*. And so, it has been clinically proven that insidious, progressive occlusion of main arteries of the lower extremity, including the femoral, popliteal, posterior and anterior tibial arteries, may take place without symptoms; and, indeed, the clinician may fail to recognize the basic vascular lesions until gangrene or trophic disorders follow a slight trauma or local infection. As shall be pointed out later, however, certain objective signs can be usually elicited, and careful examination will lead to the discovery of the condition long before grave consequences ensue.

The subjective appreciation of local deviation from the normal must needs vary with the individual's apperception and introspective psyche, as well as with his threshold of sensitiveness. Our interrogations, therefore, should be so put as to make up for the deficiencies of those who might lead us astray. Pain in the affected territory, coldness, paresthesia, liability to fatigue, may antedate by months or years, the appearance of the more easily recognizable features. Coldness of the toes of spontaneous onset, or after but slight degrees of exposure, is also a sign worthy of note. It must be remembered, however, that *pari passu* with the gradual extension of the vascular obturation, collateral paths may enlarge so that subjective symptoms may disappear. On the other hand, the liability to pain and cramps on walking may increase as time goes on, and masquerade under the guise of rheumatic pains, flatfoot ache, "cramps from varicose veins" and the like.

The signs that may be objectively elicited will be discussed in full elsewhere. They include (1) the immediate result of circulatory inadequacy; (2) the evidences of dilatation of peripheral capillaries and arterioles (rubor or erythromelia); (3) vasomotor lability or instability; and (4) trophic disorders and gangrene.

In the interpretation of the *prognostic significance* of these manifestations, we must bear in mind their intensity and extent, the duration of their existence, their constancy and especially the progressive nature of the phenomena of malnutrition. The immediate results of circulatory impairment may, as already mentioned, be so slight as to escape notice. With sudden and extensive interruptions of the current, however, pallor of the foot (or even leg) on walking, on elevation, or in the horizontal position, is a significant sign. Coldness of peripheral parts to the touch, with a distinct increase in warmth of portions more centrally located, is an important objective phenomenon. Other expressions of nutritive disorder include those more delicate changes in the skin texture, the nails and the subcutaneous tissues that are to be described in detail.

The condition of *rubor* (erythromelia) is such a characteristic manifestation as to warrant careful and detailed study. It may develop very gradually or within a very short time; it may be a permanent sign or gradually disappear; and is under the influence not only of the immediate state of the circulation of the part, but also dependent on posture.

Vasomotor instability is not a constant attendant disturbance, although well marked in some cases. Its expression may lead to confusion, and therefore, its rôle and its separation from evidences of purely hydrostatic or mechanical origin may be occasionally difficult.

Trophic lesions and gangrene, too, are characteristic results of poor local nutritive states. However, even the causation of these may not be altogether clear, whenever signs of apparent vasomotor lability seem to dominate the picture. Of the less striking, but nevertheless important effects of these

maladies, are the alterations in deeper tissues, particularly of the bones. The changes in conformation of visible parts give us a clew as to abnormalities in the subcutaneous tissues. But the condition of the bones requires elucidation with the Roentgen ray wherever there is a doubt as to diagnosis. It is noteworthy that the osseous tissues may suffer even greater absorption in some of the true vasomotor neurogenic circulatory disorders than from the more constant effects of organic vascular occlusion.

Evidences of disturbed nutrition may be hyperplastic rather than degenerative. And so hypertrophy of the subcutaneous tissues is occasionally seen with chronic cyanosis of the hands.¹

In the neurogenic or vasomotor derangements, sensory and objective circulatory phenomena may be so closely linked in onset and duration, that a causal interrelationship is often assumed to exist. The effects of the purely hydrostatic depletion, stasis or deficiency of flow (through vasoconstriction) are here also hard to separate from trophic disorders attributable to pure neurotrophic abnormalities. In short, whereas in organic occlusive disease of the arteries, a direct association between trophic disorders and circulatory insufficiency can usually be invoked in explanation, the nutritive complications of the vasomotor affections, may be under the influence of one or several different forces.

CHAPTER XIV

THE TROPHIC FUNCTIONS OF THE NERVOUS SYSTEM

The rôle of the nervous system in the production of trophic disturbances, wounds that refuse to heal, ulcers, necroses and gangrene should be thoroughly understood as far as present day knowledge permits, in order that the clinician may differentiate the neurogenic cases from those of organic vascular origin. When we speak of trophic disturbances, we can, in a broad way include not only those that are directly dependent upon poor circulation, or the action of external insults (cold, chemicals, heat, etc.), but also some of the clinical effects of nerve derangement. Classification is made difficult by reason of the fact that we are at pains to conclusively differentiate between the trophic lesions produced by external and endogenic causes. Some believe that severe cold may produce its effects only by direct action, and others attribute the tissue disturbances for the most part to the neuromyolytic effects of cold upon the blood vessels. For our purposes, it would be well to keep in mind two large categories; trophic disturbances of a nutritive or mal-nutritive nature from whatever cause, and those of purely neurotrophic origin.

Several theories have been put forth to explain neurotrophic disorders in the peripheral tissues; firstly, that the inflammation extends along the nerve until the innervated area is reached; secondly; that the inactivity induced by the neurogenic condition is responsible; and thirdly, that the anaesthesia produced by the nerve lesion results in an inability to avert injury. Numerous clinical observations, however, have shown that none of these causes must obtain. We are, therefore, constrained to accept the view

¹ See Chap. XCV, page 528.

that there is a direct trophic influence exerted on the tissues through the nervous system.

The Exercise of Neurotrophic Influences.—Several theories have been offered in explanation of the paths along which trophic influences are exercised.

One *vasomotor theory* presupposes that the tissue changes depend upon vasomotor influences. Accordingly trophic lesions may result from neuro-paralytic hyperemia, or from anemia due to neuro-irritation.

The theory of *neuroparalytic hyperemia* is based upon the supposition that in these circumstances, inflammation and nutritive disturbances occur more easily than with a normal vascular tone. Certainly experiments do not corroborate this theory; in that tendency to inflammation through experimental lesions of the sympathetic in animals has not conclusively shown increased tendency to inflammation.

The theory (Brown-Séguard) that a *neuro-irritative ischemia* is responsible for certain trophic disturbances also has not found substantiation. Of recent years some of the European authors have attributed late trophic disturbances in gangrene (after exposure to cold) to neuroparalytic lesions of the blood vessels.

It does not appear proven nor plausible that either vasomotor theory should account exclusively for trophic disturbances. Alterations in the blood content of the affected part have not been observed clinically to precede the trophic disturbances, except in those cases (thrombo-angiitis) where the nutritive lesions can be explained otherwise. Certainly in the neurotic muscular atrophies or in the neurotic glandular atrophies, or in the tabetic arthropathies, no such prodromal vascular disturbances have been noted. In short, vasomotor derangements can only be regarded as contributory causes.

The Theory of Special Trophic Nerves.—According to another hypothesis special trophic nerves are assumed to exist (Samuel¹). Perhaps the only affection which presents symptoms that would seem to substantiate such a view is that called progressive facial hemi-atrophy.

This is a disease in which the skin, as well as the bones of one side of the face slowly atrophy. According to Samuel this condition is to be attributed to an isolated lesion or paralysis of trophic nerve fibers. However, in almost all such cases other nervous derangements of sensory and secretory type, are present. The implication of other nerves, particularly the trigeminal, and in some cases also the sympathetic, are facts that warrant a modification of the above hypothesis and do not permit of the wilful assumption that specialized trophic paths are present.

In short, the existence of isolated special trophic nerve paths and centers has not been proven clinically or experimentally. Most observations and investigations, therefore, agree in supporting the conclusion that the trophic influences pass through the very same nerve paths and centers that possess other special function.

As to how the trophic influences act, a number of different theories have been advanced, and perhaps it is best to discuss these in connection with the different tissues, since their actions may not be uniform, and then to point out in what form and to what extent these tissues are subject to such trophic influences. *Of these theories, there are those that presuppose a diminution in nervous influences;* others that interpret the trophic influences as *conditions* of irritation or excitations; and finally those according to which trophic lesions depend upon *abnormal reflex stimuli* from the *periphery*.

Closed Circuit and Nerve Impulses.—It is still a mooted question as to whether direct contact of nerve elements is necessary for the exercise of nervous forces.

¹ Samuel, Trophoneurosen, Eulenburs Realencykl., XX, II, Aufl.

The Interdependence of Nerve Paths with Particular Reference to Trophic Function.—If we accept the neuron theory, we believe that the nervous system is made up of innumerable nerve units or of anatomically or physiologically specially destined and characterized individual cells. The constituents of such units are the cell bodies with their dendrites, their nuclei and nucleoli, and the axis cylinders, the latter leading into medullated or non-medullated fibers. According to the new tinctorial methods that show fibrils in the axis cylinder, the histologic unity of these nerve cells and their processes has been subject to strong criticism. These fibrils appear in the axis cylinder as long, parallel lines or threads, whilst they split up in manifold fashion in the ganglion cells, intersect and intertwine. Besides these the neurofibrils pass from one dendrite of one cell into its neighbor's.

We are still uncertain regarding the manner in which communication takes place between the intracellular neurofibrils, and those peculiar and varied endings of nerve fibers that approach the cells from the nerve fibers. We should not hold too tenaciously to the concept of an anatomical independence of the nerve units.

Be this as it may, the transmission of the nerve impulses from the physiological standpoint from one cell to another can be carried out by nerve streams that pass directly or through a gap; and it appears irrelevant as to whether direct communication is present or not.

As for the rôle of the nerve cells in the production of trophic influences, some authors have regarded those ganglia cells that are included in the heaps of fibrillar substance as having no other specific function than that of nutritive reservoirs. There have been but very few adherents to this special doctrine.

The Interdependence of Certain Portions of the Nervous System as Studied in Nerve Degeneration.—Three types of degeneration occurring in the nervous system throw considerable light upon their function and anatomy. These may be divided into the Wallerian degeneration, or Lenhossek cellifugal degeneration, the retrograde degeneration, and secondary atrophy or indirect degeneration.

1. *The Wallerian Degeneration.*—Section of a motor nerve is followed by degeneration distal to the point of the break in continuity and up to its endings in the muscle. Section of a sensory nerve is followed by degeneration up to the endings in the periphery. Section of a posterior root causes degeneration of the intramedullary course. Therefore, the degenerative process is always away from the cell (cellifugal) in the sense of the physiological direction of the impulses (towards the periphery, or caudad). It appears that the neuron theory gave a satisfactory explanation of the destruction of the axis cylinder, when severed from the cell, the accepted belief being that the neuron constitutes a nutritive entity. It is hard to conceive, however, how parts situated at great distances from the cell can obtain their nourishment through it. Indeed, the nodes of Ranvier have been regarded as points of entrance for nutritional fluids. Therefore, the trophic action of the nerve cell must be interpreted in another light, possibly as exerting such influences on the axis cylinder that enable it to attract nourishment from the neighborhood, and utilize it. The assumption that a ferment substance emanates from the cell, gives no more satisfactory explanation than the view that centrifugal impulses from the cells assure the axis cylinder of the power of nutritive assimilation. Furthermore, we cannot adhere too strongly to the notion that trophic influences are confined merely to an anatomic unity of the cell and its axis cylinder. The observations upon which the whole theory is built up do not concern themselves with single cells and their processes, but in fact we are always dealing with a multiplicity of cells and fibers. When we speak of degeneration clinically and anatomically, also pathologically, cell groups and fiber groups only are actually considered.

Concerning the dependence upon central nerve matter and peripheral fibers, observations are at hand that show that lesions in the spinal cord follow in the wake of amputation. For instance, distinct alterations in the spinal cord not limited to the white matter, but implicating the ganglion cells with diminution in size of the anterior gray horn have been observed. Involvement of the anterior or posterior tract and varying amount of implications of the white and gray substance have been observed.

Theory of Cellular Excitation.—According to Monakow it would appear that alterations in the ganglion cells, after section of the peripheral nerve, depend upon two factors: firstly, as to whether the cell is in possession of rich collaterals; and secondly, on the point of section. When the point of section is very far removed from the cell, its action is minimal as compared

to proximal interruptions. The degeneration of the cell, in his opinion, would depend rather upon the amount of functional disturbance. The degree of disturbance of the latter is directly related to the number of functional impulses that are excluded, these including not only influences from the axis cylinder itself, *but of all the neighboring nerves that are in close relation to it*. Perhaps all cells require similar stimuli for the conservation of their trophic integrity.

Section of axis cylinders causes rapid changes in the related anterior horn and ganglionic cells in most cases.

The intensity of these changes vary, and the cell may undergo a reparative process, a return to the normal occurring to a considerable extent. Whenever the cut nerves become reunited, the cells return to normal. Per contra, these undergo simple atrophy when the function is in abatement by reason of a permanent break in continuity.

2. *Retrograde Degeneration*.—In this category belong the degenerative processes that manifest themselves in a reduction of the size of anterior root fibers after amputation. Similar narrowing of the posterior root leading into the posterior tract has often been observed. Then, too, diseases of the peripheral nerves, either peripheral neuritis or the action of compressing tumors, is followed by some degeneration in the corresponding posterior roots and the corresponding posterior tract. Although in some cases these changes have been interpreted as an extension of the toxins that led to the polyneuritis, in other cases the changes have been believed to be of reactive nature in consequence of the peripheral lesions. Such apparent retrograde degeneration is not confined to the territory of the motor and sensory nerves. They have been found in the brain itself and in the centers of the optic thalami after cortical lesions.

The Reflex Theory.—Explanations of so-called retrograde degeneration throw important light on the problem of trophic influence of the nervous system. According to one view, the trophic functions of the nervous system are not automatic, but reflex in nature. Marinesco expressed the following hypothesis, in explanation of the central proximal atrophy occurring after amputation. The cause of the degeneration (in the cells and in the central stump) is to be sought in the interruption of the continuity between periphery and center. One may suppose that by irritation of the sensory nerve endings biologic changes (probably of chemical nature) are produced in the spinal ganglia, and that a trophic influence in the efferent fibers from the ganglionic cells is thereby exerted. When section of an extremity or of a nerve takes place, quantitative and qualitative changes in the impulses through the nerve ends must needs result that are no longer able to evoke the adequate trophic function; therefore, a slow progressive degeneration of the nerve fibers ensues. Just as the fibers of the central nerve stump show changes, so also the fibers which travel from the spinal ganglia to the spinal cord become altered. This explains the atrophy in the sensory sphere. According to this view, impulses travelling to the cells simultaneously serve to conserve their trophic function.

According to a supplementary view, such activating nerve stimuli do not necessarily have to emanate from the periphery, but may be of central origin. That is, other reflex impulses that are subconscious may be effective. Among these may be mentioned metabolic processes, emotion, and a variety of constantly changing and repeated, almost continuous stream of impulses of sensory and motor nature. *These serve to excite the trophic function of the cells*, and when absent, there result those atrophic alterations of the ganglion cells and their processes that have been observed.

According to still another interpretation, it is the inability to give off impulses that is the essential factor in the production of the degenerative cell changes (Lenhossek). For the conservation of the normal integrity a continuous function of the cell is necessary.

That section of the posterior root is followed by degeneration of the spinal ganglionic cells is difficult of explanation. Under such circumstances, impulses are still received, and in spite of this fact, marked derangement in the anatomical conditions of the spinal ganglion cells is noted. From this we would have to conclude that an uninterrupted flow of impulses from the cells or the cell responses, is essential for the conservation of the cell equilibrium. Every derangement of function, be it an obstacle to the reception of impulses or changes in the giving off of impulses leads to alterations in the anatomical structure of the nerve cells. Unfortunately this theory is nothing more than another way of stating the facts.

The Theory of Heterologous Stimulation.—Interferences with trophic function are said to be also due to suppression of impulses in neurons that are not in anatomical but in functional relationship. Observations on secondary atrophy would substantiate such a view.

3. *Secondary Atrophy or Indirect Degeneration.*—Under this name, Monacow describes secondary changes in the nerve fibers and ganglion cell groups characterized by qualitative conservation of the histologic elements, but distinct diminution in volume of all parts. The medullary sheath becomes very narrow, very thin, the nucleus poor in chromatin and the Nissl bodies of the protoplasm become indistinct.

This degeneration has been explained on the assumption that through the suppression of one neuron, changes take place in a second neuron that is functionally in relation with the first. As an example may be mentioned the amyotrophic condition in tabes following disease of the sensory protoneurons. So also Schaeffer would explain the changes in the anterior horn cells as due to disease of the sensory neurons.

According to this view, trophic derangements extend not only through homologous (motor-motor) but also through heterologous (motor-sensory) neurons. The condition of certain nerve fibers is doubtlessly influenced from the trophic standpoint, through systems that are in close functional and anatomical relationship.

In short, the striking peculiarity of the nervous system is the interdependence and relationship between function and structure of the cell. The function consists of the reflection of the impulses or irritations, the elaboration and the conversion of the irritant or impulse, and finally the giving off of impulses. It is even possible that disturbances in any one of these three functions may lead to localized trophic disorders. On the other hand, it is doubtful that the integrity of any unit is absolutely essential for conservation of its nutritive condition. Indeed, the neuron theory does not explain either the so-called retrograde degeneration, nor the secondary atrophy. Cassirer believes that if we consider the ganglion cells as a sort of center, that is in spatial and functional relationship with a certain number of degeneration and trophic disturbance, as upon the basis of the unity of the ganglion cell and its processes.

Nerve Influences on Osseous Tissues.—A few words concerning the dependence of the conservation of bony tissue on nerve influences may not be amiss, since trophic alterations, particularly in the end phalanges can give us valuable diagnostic information. The differentiation of primary atrophy of the distal phalanges associated with Raynaud's disease and sclerodactyly from nutritive disorders due to inactivity, syphilis, syringomyelia and secondary infection may be thereby facilitated.

The nerve control of osseous nutrition is well exemplified by the retarded bone growth of infantile spinal paralysis. There are also some clinical observations on disturbed growth of bones after peripheral nerve lesions. Gayet and Bonnet described a case in which resection of a neuroma formation in the median nerve seven years previously was followed by diminution in size of bones and rarification. A number of instances of intensive osseous changes after traumatic lesions of peripheral nerves can also be found in the literature.

Bone disease associated with diseases of the central nervous system is more common. In syringomyelia, osseous alterations are not infrequent. These are necroses particularly of the tips of the phalanges of the fingers, or diminution of their size; or, even disappearance of small bones without inflammation or suppuration. Roentgenograms may show bone atrophy and lightening of the bone shadows, both of the diaphysis and epiphysis. Even enlargement of bones has been reported without the presence of acromegaly in cases of glia changes in the spinal cord.

Fragility of bones, too, occurs in paralytics, although this has been interpreted by some as due to atrophy of inactivity. A rarifying process may make the bones brittle when tabes is present, and liable to spontaneous fracture.

There are cases in which after trauma of an extremity without wound or suppuration, marked trophic disturbances appear. These may be accompanied by slight vasomotor symptoms and sensory irritative phenomena, but deficiency manifestations in the sensory nerve domain are absent. Here it is believed that the trophic disturbances have a reflex cause through excitation of the sensory apparatus. Cassirer mentions a case of Sudeck¹ in which after injury of a hand, swelling, redness, pain and restricted motility resulted. The X-ray picture presented the characteristics of *bone atrophy* with clarified bone substance and typical atrophic changes in the carpal bones. Even osteophytes are said to occur as an expression of continued reflex irritation.

Characteristic in lepra are the resorptive and degenerative processes in the peripheral phalanges with mutilation of the parts. The lime disappears hand in hand with atrophy of the rest of the bony parts, and corresponding changes in the soft parts. The bony resorption in these cases is so characteristic and so extensive, that it can hardly be mistaken either for the very minimal changes of Raynaud's disease or sclerodactyly; nor can it be readily confused with the bone and joint destruction associated with perforating ulcer, arteriosclerotic ulcers and gangrene.

The cause of the bony changes is said to be a trophoneurotic one due to lesions in and about the peripheral nerves.

Trophic Influences on the Vessels.—If such a relationship exists, it is all the more important by reason of the secondary effects that could be thereby transferred to the tissues supplied by the vessels in question. Lapinsky claims to have demonstrated structural changes in the walls of arteries after section of the vasomotor nerves. Cassirer accepts the experimental work of this author as reliable even though others (Jores) could not offer confirmatory facts.

As for the manner in which vessel alterations are dependent on the vasomotor nerves, satisfactory explanations are difficult to find. In how far do these changes result from the absence of functional impulses? Or, to what extent are direct nutritive stimuli responsible for conservation of anatomical integrity? A complicated mechanism is put into action when vasomotor nerves are experimentally cut off. For, the induced dilatation of the vessel permits of new mechanical hydrostatic or circulatory forces to come into play and possibly exert an effect on the arterial walls. Perhaps the therapeutic results of future operations on the periarterial sympathetic fibers (Leriche) will throw additional light on this obscure subject.

¹ Sudeck, Monatschr. f. Unfallheilk., VII, 50, 1910.

CHAPTER XV

TROPHIC DISORDERS OF THE SKIN

Neurotrophic disorders of the skin include all those regressive, hypertrophic, and so-called inflammatory changes dependent upon the nervous system. The skin and the nervous system are brought into communication through those sensory nerves in which fibers of the cerebrospinal and vegetative systems are contained. Probably the sensory nerves *per se* have no direct influence upon the vital functions of the skin. When the sensory paths are interrupted, the parts are placed in jeopardy, insofar as injurious moments do not come to consciousness. Such is the case in syringomyelia and in interruptions in the continuity of the peripheral nerves. As a rule, trophic changes associated with sensory disturbances depend exclusively upon lesions or irritations of the vegetative nervous system, whose paths and centers are in intimate relationship and contact with the sensory fibers.

The distribution of blood, and therefore the nutrition of the skin, is under influence of the nervous system through the vasomotor paths. And so, a continued spasm of vasoconstriction and so-called neurogenic stasis may cause functional derangement of the skin.

The immediate effects of injury of the peripheral nerves demonstrate that the cutaneous vessels may functionate independently of the nervous system. Later on, however, distinct disturbances in the blood supply appear, such as anemia or cyanosis; and with this, other changes in the surface of the skin, namely, purplish discoloration, thickening, changes in the nails and glossy skin. The latter are evidences of dystrophic or maltrophic alterations in the integument. And so also, the vascular responses to external stimuli or conditions suffer a change. Under such circumstances there is a tendency towards severe regressive or degenerative changes. Inflammatory processes are intensified and the ability to heal is diminished.

In addition to the vasoconstrictor and dilator paths, vasosensory fibers course in the peripheral cutaneous nerves. They are important in the nutrition of the skin. For we can only then expect an orderly nervous regulation of the blood distribution when a harmonious and reciprocal association of the vasomotor and vasosensory impulses obtains.

According to some it is hardly necessary, nor in accord with any observations to postulate the existence of a separate trophic nervous system. In cases of nerve lesions trophic disorders may be absent for years. The origin of the so-called glossy skin has been explained upon the theory that the vasomotor relations have been disturbed. A thickened, brittle skin with hyperkeratosis is also noted in cases of peripheral nerve lesions and in localized spinal diseases, such as syringomyelia.

Of the so-called inflammatory types of trophic disorders herpes zoster is an example. This is the only one of the trophic disorders in which certain distinct anatomical changes in the nervous system have been demonstrated. There are hemorrhagic inflammatory processes in the spinal ganglia.

Certain cases of circumscribed edema and urticaria may be of neurogenic origin, whilst in other cases a toxic cause is responsible. That neurogenic cases can exist is proven by the examples of urticaria of psychogenic or reflex creation demonstrable after the passage of bougies in the urethra; and also in dermatographism. The exact nature of the responses depends to a considerable extent upon the predisposition of the skin, and upon the individual.

Trophic disorders of the nails manifest themselves in irregular growth. The nails may become plump, easily torn, show furrows, may degenerate, and later may break up. External injuries or insults often give rise, in predisposed individuals, to inordinate responses on the part of the skin. Such a predisposition to trophic disorders is exhibited by certain weak cutaneous structures in cases of myelitis or nerve injuries or lesions.

A number of skin lesions have been regarded as due to trophoneurotic causes. Amongst these may be mentioned: *malum perforans*, *acute decubitus*, *skin changes of peripheral nerve disease*, and those associated with *syringomyelia*. All of these should be carefully studied before we can possess correct diagnostic appreciation of the varied clinical pictures of gangrene.

Mal perforant is fully discussed in Chap. LXXXIII. To what extent this process owes its character to nerve lesions has not as yet been conclusively proven. In some cases at least we may accept the existence of derangement of sensory nerves as well as of vessel reflexes.

As for *acute decubitus*, views differ as to the rôle of mechanical infectious or neurogenic influences in its causation. A careful perusal of the literature permits us to cull a few authentic examples of undoubted neurogenic nature. In such the skin necrosis is said to have developed a few hours after the onset of the nerve disturbance (hemiplegia and hemianesthesia). That immediate skin changes can follow cerebral lesions is recorded in the reports of pemphigus-like eruption in the paralyzed areas, extensive bleb formation in territories with sensory and vasomotor disturbances, etc. In some cases "decubitus" is the product of a combination of factors, pressure, vasomotor weakness of the skin, and infection.

Another manifestation of the relation of the nerve and cutaneous systems, is the *glossy skin* described by Weir-Mitchell. Not greatly dissimilar are some of the remarkable changes in the integument occasionally seen in the feet, when slowly progressing but vast arterial obstructive lesions of arteriosclerosis impair the nourishment of the parts. Also, in rare cases of thrombo-angiitis obliterans, a condition of the skin of the hands, with trophic lesions of the nail beds, without ulceration, may give deceptive pictures.

In *glossy skin* the skin is red, thin, shiny and stretched. With it there may be burning sensations or neuralgic pain. The hair and rugae of the skin may be absent, whilst sensation may be conserved. It is important to note that this lesion appears when only partial section or interruption of nerve continuity in the territory has taken place.

If the cutaneous disturbances correspond to the territory innervated by certain nerves, their neurogenic nature is usually easy to recognize.

A word may not be amiss regarding neurotrophic skin changes attending *syringomyelia*, which must also be occasionally considered in differentiating trophic disorders and gangrene. Here the lesions are usually associated with motor, vasomotor and sensory derangements. Nor can we always establish a causal relationship between the cutaneous changes and other evidences of nerve lesion, since the former may antedate the latter.

As for other lesions, such as *herpes zoster* and *multiple neurotic gangrene* of the skin, these would seem to indicate the existence of a close neurotrophic relationship. In the case of herpes, Head says that the eruptions are not produced by disturbance of special trophic nerves, but by intense irritation of cells in the ganglia, which normally subserve the function of pain. Probably irritation of sensory end-neurons are responsible for the trophic changes in the skin. Cassirer suggests a reflex disturbance of the vasomotor nerves through sensory impulse.

In multiple neurotic gangrene of the skin such vasomotor derangement has also been considered possible, the reflexes being either of toxic, electric or psychic nature.

The so-called *trophedema* is a hard, white, painless edema of rather chronic course. It is usually observed in youth and is progressive. It is demarcated by a sharp circular line in a segmental fashion, being limited to certain parts of the limb, and is not infrequently a familial disease.

Pathogenesis of Neurogenic Gangrene.—The question as to whether gangrene may result solely from changes in, or functional derangement of the nervous system without reference to effect of vasomotor spasm, has been a much mooted one. As for the peripheral nerves, evidences are lacking that these are the seat of degenerative changes either in Raynaud's disease or in other cases of spontaneous neurotic gangrene. When they are reported as having been present, they are usually not the cause of the gangrene, but secondary, and result from the same forces that are productive of the gangrene.

As regards the central nervous system, it is known that marked nutritive disturbances of the skin and its adnexa can be associated with the central nerve changes, as in syringomyelia. Indeed, gangrene has been observed complicating even gliosis.

Cassirer is unwilling to accept the purely ischemic theory or that of angiospasm as sufficient to explain the gangrene in Raynaud's disease. This view receives additional confirmation in the manifestations of gangrenous herpes and in the disease of *multiple neurotic skin gangrene*, where irritation of the vasomotor nerves is believed to occur. Indeed, Kreibich¹ was able to produce angioneurotic inflammation experimentally, and also, patches of gangrene in the latter affection with the use of faradic current and other irritants. He suggests that the nerve impulses excite paralysis of the vessels through irritation of the vasodilators with consequent edema, exudation, and necrosis; and that the necrosis is due to increasing pressure of the exudate.

These observations, however, cannot be invoked in explanation of the Raynaud complex, since, in the latter, vasoconstrictor, and not vasodilator irritation exists. Whilst Kreibich and others would interpret the necrosis as the result of mechanical effect of an exudate of vasomotor origin, Cassirer rejects this assumption, believing it more plausible that there is a direct trophic action through the nervous system on the tissues; and with such a theory he would interpret gangrene associated with both vasodilator (multiple neurotic gangrene) and vasoconstrictor (Raynaud) impulses. Enough data are at hand, however, irrespective of which view may be correct, to warrant the belief *that neither angiospasm nor ischemia satisfactorily accounts for all types of neurogenic necrosis or gangrene*; for this occurs where vasodilatation has been shown to exist. It may be accepted therefore, that a primary gangrene of the skin may take place by reason of alterations in, or functional derangement of the nervous system.

A new French school has arisen that would regard even trophic ulcers of traumatic peripheral nerve origin as explicable by the theory of deranged vasomotor function. Thus the trophic ulcers complicating transverse injury of the sciatic nerve² have been recently attributed to vasomotor reflexes produced by a neuroma of the nerve's proximal end. According to this theory the active proliferation in the neuroma is the point of departure of vasodilator reflexes that augments the existent circulatory disturbances. By virtue of this effect minimal local peripheral traumata may give rise to sero-sanguinolent exudation in the connective tissue meshes, in which the dilated capillaries have lost their function and that consecutive cutaneous necrosis and ulceration ensue.³

¹ Kreibich, *Die Angioneurot. Entzündungen*, Wien, 1905.

² See Chap. on Trophic Disorders in Diseases of the Peripheral Nerves.

³ Leriche, *Lyon Chirurg.*, 18, 1921, p. 43-44.

Summary.—The passive tissues too, such as skin, bones and joints, are under the control of trophic nerve influences. It would seem that a specially attuned reflex mechanism is here essential for the harmonizing of their nutritional condition and their specific functions. Cassirer offers the following views: Pathologic changes of innervation exert a more injurious effect on the nutrition of tissues, than when nerve impulses are completely in abeyance. Excitation of sensory nerves calls forth marked reactions in vascular innervation. Although the tissues, in general, are trophically innervated, they may continue spontaneously to make up for nutritive defects. The special trophic impulses would only then be significant when the nourishment of the tissues is under special strain, as in the presence of unfavorable conditions such as continued pressure, and unusual desiccating influences. But when the normal innervation becomes pathologically altered through special irritants, the nourishment of those tissues that are within the anatomic and physiologic boundaries of the exciting impulses, may be reflexly modified thereby; and as long as the special irritants continue. So that accordingly it is not an absence of innervation, but rather *a pathologically deranged form of nerve impulse that comes into consideration in the development of trophic lesions*. Indeed Leriche has recently expressed the hypothesis that trophic ulcers after nerve section (Chap. XCI) may be caused by reflexes set in motion in the neuromata of the nerve's proximal end. In an analogous way, intense symptoms may be produced by the constant irritation of posterior roots by a new growth, and manifestations may be wholly lacking with complete destruction of such posterior roots.

Other authors have expressed the opinion that when nerve impulses are interrupted, the nutrition of tissues goes on, but with diminished activity. Under such conditions only special demands upon the functional activity of the nerves may bring deleterious changes. The tissues are believed to become more sensitive, so that increased pressure may lead to necrosis as in cases of myelitis; or, the insensitive cornea may be injured through the very slightest external traumata with resulting ulcer formation. In many examples of trophic disorder, the occurrence of a trauma might be regarded as sufficient to explain the condition, since under normal circumstances the tissues of the body demonstrate their ability to resist external influences and conserve their nutritional integrity. Slight external irritants, when followed by trophic derangement, indicate a *disorder* in trophic innervation (trophic function).

Whenever the skin cannot meet the exigencies of the normal external accidents and stresses and reacts with evident nutritive disorder, we are warranted in assuming that impairment of the neurotrophic function exists. Conditions of deranged trophoneurotic function may escape our cognizance, unless each set of the motivating factors resulting in manifest impairment of tissues be carefully analyzed and weighed.

Most authors agree that the existence of isolated trophic nerves is not supported by present evidence. That the nervous system exercises a trophic function cannot be denied, and the trophic influences doubtlessly pass through paths serving other purposes. The skin receives the trophic impulses by way of the sensory and vasomotor paths, and may travel in a direction opposed to the usual impulses travelling through them. The action of reflexes by way of the sensory to the vasomotor paths is also of great importance in determining nutritional effects.

CHAPTER XVI

GENERAL CONSIDERATIONS OF THROMBOSIS

Forms of Thrombi.—To elucidate both the pathological and clinical phenomena observable in cases of gangrene, a clear concept of the process of thrombosis is essential. The practitioner should not be satisfied with a loose notion regarding the pathology and causation of the thrombotic lesions that partly or completely occlude the arteries and veins.

The coagulation and the loss of the fluid state of the blood, when it occurs during life, becomes one of the morbid processes. For the recognition of thrombosis as a disease, we must differentiate *intra vitam* and *postmortem* clots. Although the word *thrombosis* has been employed in a wider sense to include also the intravascular accumulation of living cells of varying types of tissue complexes and of bacteria, the presentation of this subject will be restricted to descriptions of *agglutination*, *conglutination* and *coagulation* of the blood elements, with the formation of clumps or solid masses of various types and forms.

The intravascular solidification of the total blood in a vessel, or of any of the component parts in the living organism, is the result of changes in those factors which under physiological conditions preserve its fluid nature. These factors are the physical power of the blood circulation and the chemical constitution of the blood. The blood flow (circulation) can undergo changes by reason of either general or local disturbances in the blood pressure, as well as through alterations in the structure and capacity of the vessel wall. The chemical composition of the blood depends upon the intrinsic vital function of the blood cell as well as upon the action of the vessel wall. But both the mechanics and the chemistry of the blood may suffer change through the action of solid or fluid bodies of alien nature that penetrate into the blood. These considerations would lead to a differentiation into *mechanical* and *chemical causes of thrombosis*. It is difficult, however, to strictly separate causal moments.

Authors differ as to whether all thrombi represent some form of decay (necrosis). According to some, thrombosis should be regarded as a form of intravascular blood necrosis, and that in the process following mechanical or chemical causes, there form certain materials made up of single or a combination of confluent blood components.

The word *thrombosis* signifies plug formation within the blood vessel, leading to partial or complete closure of the vessel lumen.

Various conditions lead to thrombosis. The following types have been described: (1) *coagulation* with separation of a solid fibrous (fibrinous) substance (clotting); (2) an aggregation of various morphologic constituents or *agglutination*; (3) the separation and cohesion of certain elements, called *conglutination*. The healing and degeneration of these elements in the latter process has also been called *congelation*.

The determining factor in thrombus formation seems to be the aggregation of elements. This may be brought about through the influence of the vessels themselves (injury of the vessel wall), through the action of the blood elements, or through agencies altering the blood elements, through hemolysis, precipitation, agglutination or destruction. Coagulation or clotting then follows as a secondary phase, and is rarely primary.

The distinction has also been made between pure conglutination thrombosis, in which the separation and aggregation of elements is essential and determining, and a combined thrombosis, of the clotting type, called *coagulation thrombosis*.

Thrombi form because of impairment of the blood stream, injury of the vessel wall, or changes in the blood composition.

Types of Thrombi.—*White thrombi* may develop in flowing blood from the heaping up of platelets or leukocytes, or both, with or without fibrin formation. When, with the blood at a standstill, the red blood cells participate particularly, a red thrombus usually combined with a white one (mixed thrombus) is formed. Such segregation of blood platelets from leukocytes can result from mechanical factors or chemotactic influences. Of the mechanical factors, centrifugal dispersion or confluence in wave nodes may be mentioned; chemotactic forces cause the attraction of leukocytes into platelet centers, as the result of chemical changes in the vessel wall. When the elements that participate undergo death, they form a coherent, colorless mass that offers resistance to the blood flow, and simultaneously delivers a ferment necessary for the coagulation of the fibrinogen of the plasma.

White thrombi can be made up of pure platelets, but only so when they are recently produced; or, where by reason of the strength of the stream, deposition of leukocytes and fibrin is prevented. This occurs in the aorta over atherosclerotic patches. Usually white thrombi are made up of platelets and leukocytes, the leukocytes being attached to a groundwork of fused platelets. Fibrin and red blood cells are admixed. When white blood corpuscles preponderate, then we speak of a *leukocyte thrombus*, but platelets are always present. The white thrombus is the typical segregation (*Abscheidungs Thrombus*). It is formed when the vessel wall is injured, without added circulatory disturbances; or it can constitute the essential structure of mixed thrombi.

Red thrombi occur either when there is rapid coagulation, or when the stream is markedly arrested or retarded, usually over a deposit of white thrombus in a retraded stream. In the red thrombus there is a rich network of fibrin with enmeshed red and white blood cells, which are not equally distributed. The red thrombus is particularly a coagulation thrombus and its loose structure permits of the tearing off and the transportation of fragments.

Mixed thrombi form the greatest percentage of all. They are made up of red and white portions (with head and tail, Aschoff).

Hyaline thrombi are found in small veins and capillaries as complete homogenic bodies, or diffusely filling the lumina. They are made up either of fibrin plugs or of a homogeneous mass of platelets and leukocytes. Toxic substances such as serpent venom, ferments, the products of the influence of cold and heat, mushroom poisoning, and the toxins of eclampsia, infectious diseases, (diphtheria, pneumonia, scarlet fever) have been known to produce these plugs. They are not so apt to occur in the extremities; more usually are they observed in the kidneys, intestines, lungs and brains.

Blockage of the small vessels may be produced by the *spodogenic thrombi*, where precipitates and destroyed fragments of blood corpuscles fill the lumina. Poisons such as lead, anilin and the absorption from burns, are the causes. A similar condition is produced through sudden hemolysis and after blood transfusion, when so-called shadows of blood cells (thrombi) or platelets and leukocytes fill the vessels.

CHAPTER XVII

THE FORCES ENGAGED IN THROMBUS FORMATION

Coagulation and Agglutination—These must be differentiated. They will be described as they occur outside of the vessels, and then as they appear in the cadaver.

Extravascular Coagulation.—Microscopic observations of the first changes in a fresh clot, of blood (hanging drop) kept in a moist chamber, may be summarized as follows: The platelets agglutinate and accumulate in small heaps, in which the contour of the individual platelets shows dissolution of their peripheral margins. The platelets stick together and to the glass chamber. The agglutination of the red blood cells into the coin-stack form takes place simultaneously, and the rolls sink gradually to the lowest part of the drop. Later they fuse to such an extent that they form solid bodies simulating hyalin thrombi. Shortly after the process of agglutination, the deposition of the fibrin elements takes place. This probably depends upon the breaking-down of the platelets. At the inception of the process, the ultra microscope shows fine linear crystal-like threads which grow under the eye of the observer, and increase in number. The fibrin masses in the hanging drop usually show at the very beginning a relationship to the platelets radiating from these. Then the crystalline form becomes lost and the fibrin attains the appearance of threads, thicker in the center than in the rest of their course.

In sterile tubes, if coagulation is rapid, the red blood cells may be thrown out at different levels, giving the clot a variegated appearance. If agglutination and gravitation are absent, the blood may solidify into a homogenous red column. The process of coagulation begins at the periphery and advances towards the center. Later the coagulum contracts with the expression of clear serum. This filtration takes place through a dense fibrin reticulum that allows neither red nor white blood cells to penetrate.

In the cadaver, coagulation of stagnant blood is modified through the continuance of a certain degree of inhibiting action of the inner vascular walls. Its process is slower and incomplete as compared with extravascular coagulation. Even if an abnormal amount of ferment is present in the capillaries and small vessels (as in pneumonia) coagulation does not take place. Inhibitory influences exerted through the vessel wall are held accountable.

Whilst coagulation incited by a foreign body takes place away from the periphery (as in the glass tube), early clotting in the cadaver is seen in the central portion of the blood column, the clot being separated by a layer of fluid from the vessel wall. The inhibitory process is believed to be due to injury, and deterioration of fibrinogen and fibrin ferments.

Between the one extreme of fluid blood, and that of delayed coagulation (cadaver) with its homogenous red clot, there are manifold mixtures of a bacon-like clot (*speckgerinnsel*)¹ with the red masses or *cruor*. The mixtures vary in that bizarre layers, combination clots, islands, inclusions or white clots are enclosed in the red portion. Evidently in the cadaver the coagulation takes place more slowly, at varying rates and at different points.

The red post-mortem clots (*cruor masses*) have the general appearance of the clot *in vitro*. Microscopically there is very slight platelet agglutination. The more dense the coagulation, the denser the fibrin net work, and the more complete is the absence of the fibrin centers. In the post-mortem clot the fibrin is exhibited throughout and shows distinct platelet centers. In rapid coagulation, there is probably a sudden invasion or saturation of the blood with fibrin ferments. This is artificially producible through the injection of tissue juices. The fibrinous network may then become so dense, that its interstices are smaller than the red blood cells. As a result, mechanical breaking-up of the cells may ensue when the fibrin mass contracts. Where there is slow coagulation as in the bacon-like clot (post-mortem), the absence of erythrocytes with the coarse platelet centers is noteworthy.

The Process of Agglutination.—The agglutination of the platelet is the signal for the rapid excretion of fibrin. So also blood whose red cells have a special tendency to agglutinate, is apt to clot rapidly, although no morphological relationship between fibrin formation and the agglutinating red blood cells is demonstrable. Substances that inhibit agglutination also diminish

¹ A term given to post-mortem clots in which the red blood cells have fully gravitated.

fibrin coagulation. However, the two processes of agglutination and fibrin clotting cannot be regarded as identical, since either can occur independently.

Agglutination of platelets, and less frequently of erythrocytes occurs; it is absent altogether in the case of leukocytes.

Agglutination represents a disturbance in the normal repulsion between corpuscular elements on the one hand, and the surrounding plasma on the other. Spatial conditions even with chemical integrity of the elements, may play a rôle in the production of agglutination. Thus, when, by virtue of mechanical conditions the cellular elements are approximated, the quantity of the inhibiting fluid between them may not suffice to prevent a tendency to cohesion. It is this mechanical relationship that may be a factor in the production of thrombi of mechanical etiology; and it throws light upon the importance of movement in the fluid, for the conservation of the blood.

If we believe that agglutination occurs by reason of dissolution of very delicate surface coverings about the erythrocytes or platelets, we must also accept the view that the microscopic cell limitation is only the boundary of the solids, but not of the fluid constituents. According to Beneke, when no cohesion of cells occurs, any normal process of attraction that may exist is inhibited by the opposing forces in the surrounding plasma. Two forces are apparently necessary for agglutination, firstly the specific function of the corporal elements, and a contrary force emanating from the blood plasma. From the corpuscles, streams of fluid matter are supposed to emanate. The production of a cohesive surface substance can be increased. Foreign bodies are known to have such influence on the platelets, and overproduction of adherent or cohesive substances resulting, implicating more and more new platelets, and attracting these to the incipient conglomerates. Chemical injury of the platelets leads to overproduction of this surface substance, or to destruction of platelets even without contact of a foreign body.

Fibrin Coagulation.—This is a complicated process in which a fibrous substance, called fibrin, separates out from the plasma in the form of a reticular mass, and unites the corporal elements of the blood into a solid mass.

In the blood plasma there are fibrinogen, thrombogen and calcium salts. Thrombogen is the incomplete antecedent of the ferments, and is converted by the activating substance thrombokinase into the effective coagulating ferment thrombin. This can occur, however, only in the presence of the calcium salts. This thrombokinase originates mostly out of the blood platelets which agglomerate at the incipency of the clotting process, break down and form the center of radiating fibrin formation. Possibly leukocytes also participate in this action. Ordinarily for the creation of thrombokinase out of platelets or leukocytes, the latter must leave the vascular channel, and in this case some of this kinase is also delivered from the salt of the wound surface. Through the action of thrombin (derived from thrombokinase, plus thrombogen) upon fibrinogen, the latter is broken down into fibrinoglobulin and fibrin.

In the vessels themselves the intact endothelium of the intima is supposed to inhibit clotting, partly in that the smooth surface exerts no irritation upon the elements that deliver kinase, and partly in that it forms an anti-clotting, inhibiting substance antithrombin.

More recently the following views have been expressed regarding coagulation (Bordet¹). The two so-called mother substances active in coagulation are cytozym—a lipid derived from the tissue cells and blood cells; and serozym present in the serum. These are the precursors or mother substances of thrombin and prothrombin.

Serozym is easily destroyed by heat; whereas cytozym, the active principle of platelets resists even 100° C. without losing its properties. The latter also exhibits in extract the characteristics of lipoids, especially lecithin.

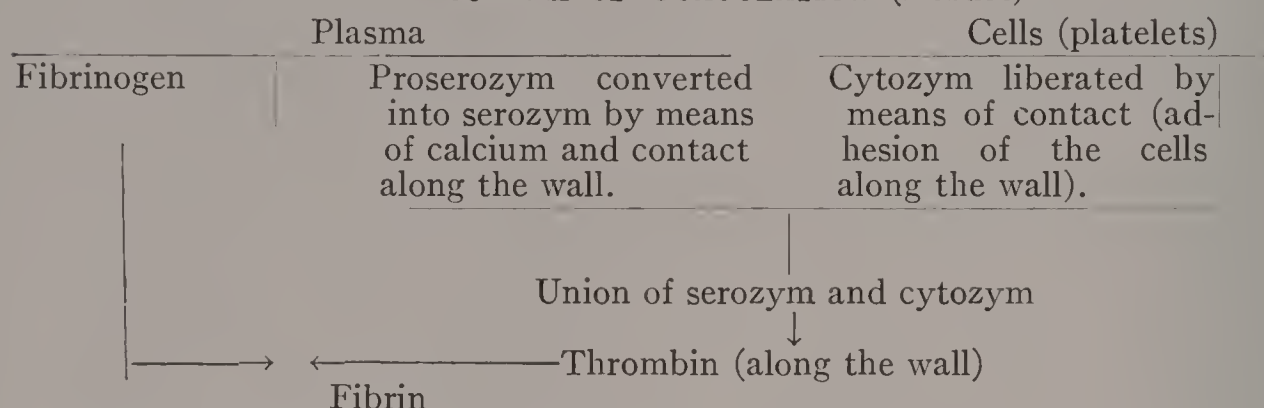
Bordet believes that cytozym and serozym unite in a manner similar to the union of toxins and antitoxins, not from true chemical affinities, but from contact or molecular adhesion. Serozym found in the serum is not there in the same condition as in plasma. It is incapable of reacting at once with cytozym in plasma. In other words, plasma contains a proserozym instead of the active serozym, so that one of the first phenomena of the whole process

¹ Bordet, Harvey Lectures, Oct., 1920, p. 36 (Lippincott).

of coagulation would be the conversion of proserozym into a body capable of uniting with cytozym.

In short, the process of coagulation may be thus summarized: Plasma contains fibrinogen and proserozym, the latter being converted into serozym by means of calcium and contact along the wall. The platelets deliver cytozym, which is liberated by means of contact adhesion along the vessel wall. Through a union of proserozym and cytozym (the former converted previously into serozym) thrombin is formed; and this, with the fibrin derived from fibrinogen, brings about coagulation.

SCHEME OF COAGULATION (Bordet)



contact and calcium no more necessary).

The degenerative susceptibilities of the blood platelets towards certain insults and their consequent tendency to clotting, are matters that become easily comprehensible.

The importance of the platelets in clotting can be studied by noting the character of radiating fibrin formation (fibrin stars). Such irradiation centers formed by the fibrin and emanating from the blood platelets are now well recognized. They are no longer suspected as being merely the consequence of fortuitous inclusion of platelets in the fibrinous network.

However, close relationship between clotting and platelet fibrin formation cannot be altogether limited to these bodies. For example, leukocytes and other cells (endothelial, Zenker¹) can embody fibrin forming forces. The grouping of fibrin about such cells in inflammatory foci speaks for this assumption. But a special condition of the tissue fluids and cells is necessary to evoke the development of their coagulins, or to activate these.

Both the quantity of ferment and the circulatory conditions play a clear rôle in the clotting process. Küster² was able to show that the clot could be modified artificially according to the amount of fibrin ferment added, the delicate ones corresponding to smaller quantities, the coarser clots to the use of larger quantities of ferment. The dilution of ferment through the circulation is, therefore, of importance in intravascular clotting. In ordinary life and under normal conditions (in which the ferment is probably present only in small quantities) the circulation is active in producing a dilution up to a point where the ferment is impotent.

Fibrin formation occurs in two varieties, in a reticular type of clotting, and in the form of true crystallization. Since authors differ as to the exact nature of the processes and division into such categories, it must be admitted that the exact limitations of crystalline and amorphous forms are not always possible.

Fibrinolysis is believed to be a normal attribute of certain cells, since a fibrin network may disappear. The breaking down of fibrin occurs more rapidly in the cadaver than in vivo. Just what particular kind of ferment is at work, whether it is a proteolytic ferment of the leukocytes, or endothelial cells is not known.

Antithrombin which inhibits clotting, is a constant product of the vascular wall, and may be regarded as a sort of vital reaction opposed to the chemical influence of the blood. Blood collected from organs containing numerous capillaries and relatively slow circulation, when taken from the living or the cadaver, has a tendency to remain fluid. Some authors claim to have found antithrombin in the liver after washing the latter and after transfusing this organ with arterial blood, anticoagulating properties then appeared in the transfusate

¹ Zenker, Ziegler's Beitr., XVII, 1895.

² Küster, München. med. Wchnsch., 1911, No. 46.

Lipoid substances, or according to others, phosphatid substances containing C. N. and P. are said to be responsible for the diminished coagulating powers. An observation of no mean importance is the relative lack of clotting in the capillaries.

Source and Quantity of Fibrinogen.—This does not seem to be produced by the blood corpuscles, since in defibrinated blood no new fibrinogen is elaborated upon standing. In an animal that has been thoroughly bled and transfused with defibrinated blood, the fibrinogen formation may attain or exceed the normal (Dostre & Mathews). Simultaneously the blood platelets also make their appearance, so that the fibrinogen has been considered as arising either from the vessel wall, or from the platelets. The latter is unlikely, since the lymph may contain fibrinogen without platelets. Therefore, the excretion and quantitative control of fibrinogen in the blood and lymph seems to be a specific function of the tissue cells. The kinase or coagulin production is a function of the living tissues, particularly of the platelets and leukocytes. Other cells, such as connective tissue cells, may participate.

Congelation.—In addition to cell agglutination and fibrin coagulation there is another type of phenomenon which is often associated with thrombosis, namely, the hyaline conversion of albuminous bodies of various forms. This phenomenon has been called *congelation* as a substitute for other terms—hyaline degeneration, and coagulation necrosis. This process, however, occurs only in dead material, even though this material forms but a part of the respective cell or intracellular substance (intracellular hyaline degeneration). Nor does it occur in every form of necrosis. The conditions for its development are more favorable in the living organism than in the cadaver. The exact nature of the process is not well known, some believing that a proteolytic ferment is at work.

CHAPTER XVIII

PHYSICAL EXPLANATIONS OF THROMBOSIS

For a comprehension of the causation of gangrene of the extremities, it is well to be acquainted with the present status of the question of thrombosis. Much discussion has arisen since the time of Virchow as to the importance of the infectious or mechanical factors in the production of thrombosis. In his day the mechanical effects of slowing of the blood stream was regarded as the all important factor. The tendency of late has been to stress infection as the deciding factor.

According to Aschoff¹ the concept of thrombosis can be clarified by a study of other physical processes with certain similarities.

The Appearance of Thrombi.—From the pathological point of view a thrombus is any obstructing intravascular mass that arises *intra vitam*. Thus we can differentiate *blood thrombi*, *tumor thrombi* and *parenchymatous thrombi*. We are merely interested here in the blood thrombi.

These latter are characterized by their distinct stratification, by their friability and undulatory nature of their surface; and, are differentiated from post-mortem thrombi by organized adhesions to the vessel wall.

In a well developed thrombus parts differing in color are recognized. The proximal portion or head portion is usually pale or a white thrombus. Adjacent to this, the neck portion is mixed in color, and the peripheral part is dark red. The head may be very small, whilst the tail often measures many centimeters. Such are their usual appearances in the venous system. The red thrombi are only found where the white portion obturates the vessel.

¹ Aschoff- Beitr. z. Thrombosefrage, Leipzig, 1912.

The red portion may be absent in parietal thrombi, the white portion occasionally growing to considerable length in a continuing circulation. The white portion is the essential part of an autochthonous thrombus, and is the real causal factor in the whole process, whilst the red portion is only accidental. A pure red thrombus without a head portion is a rare exception. Such is the description given by Aschoff for the ordinary thrombus. That these rules do not obtain in inflammatory thrombi, such as are seen in thrombo-angiitis obliterans, will be learned in the section on that affection.

Macroscopic and Microscopic Appearances of the Caput.—Certain characteristic appearances of the surface of an autochthonous thrombus correspond to the internal structure, and have lead Aschoff to propose certain explanations of the method of its origin. The fluted or reef-like markings, and the reticular and streak-like shadings seen in the caput and neck portion of the thrombus are considered characteristic. An explanation of these markings is offered by this author that should lead to a correct concept of the origin of this type.

A longitudinal section through the head and neck portion of the thrombus, shows that the above described superficial reef-like elevations are but the summits of beams or skeleton structures. These are coralliform or frame-like joistings, that form the supporting structures of the whole thrombus mass. This framework is constituted by the heaping up of blood platelets in a fine granular mass. Above these beams or girders a fine layer of leukocytes is disposed, whilst in the interstices between the main support, the red blood cells fill out the structure.

The beams themselves are disposed to each other in a regular fashion, separated by interspaces of varied size, and with fine branches passing upwards and downwards. As we approach the caput, the blood-filled interspaces become narrower, until the supports fuse together into the white summits of the thrombus.

The fibrin is almost absent in this whole structure. When it is present, it is found at the margin where the platelet structure is in contact with the red blood.

When it was shown (Deetjen¹) that the blood platelets are independent elements assisting in the circulating blood, it became comprehensible, that only in flowing blood could such masses of blood platelets be deposited, as are to be found in the above described framework of thrombi. The platelets do not originate from white or red blood cells, but are independent elements arising from the giant cells of the bone marrow and in the spleen. The platelets show a finely granular center, and a clear peripheral zone. They are detached from the giant cells, megakaryocytes and attain spontaneous mobility. These megakaryocytes of the bone marrow have been seen to interpose pseudopods into the capillary blood channels, and in this way the transference of the blood platelets into the circulation comes to pass.

It has been shown that when a section of vessel is tied off by ligation no platelet formation could be observed even after the employment of caustic irritation, whilst a typical platelet thrombus develops under such conditions in a vessel in which the blood circulates. A *platelet thrombus*, therefore, is regarded as arising in flowing or circulating blood.

Formation of the Thrombus.—The framework of this type of thrombus is composed of a lamellar system (Fig. 41) with the elements more or less parallel, either transversely or obliquely disposed to the long axis of the vessel. In this sense, the structure resembles the effect of the ebbing tide on the fine sand of the ocean beach. A similar step-like line formation is produced by the flowing blood, the platelet masses forming the delicate lamellar system. Just as in slowly running water, finely divided elements may be deposited in a regular way so as to form reef-like formations, so in the blood vessel, platelets are deposited in the above-described framework. As the blood continues to flow, more and more platelets are attached, and further elaborate the structure. In the oldest portion of the platelet system, the renewed deposits are greatest, and finally the time arrives when the interstices of the lamellar system (in the oldest portion of the thrombus) become so minute that the blood stream becomes slower and slower, and finally ceases. At this moment the primary thrombus formation has attained its finality,

¹ Deetjen, Ztschr. f. physiol. Chem., Bd. 65, 1909.

since no more platelet masses are added and its primary growth can continue no further.

The leukocytes in this system follow the usual laws according to which the specifically lighter white blood cells take the peripheral zone of the stream. Here, since the stream is divided into numerous sub-streams by the regular structure, the leukocytes follow the same law and are deposited along the walls of the structure.

This is the manner of formation of the head portion of the typical thrombus (Aschoff¹).

The *tail portion* of the thrombus in which a platelet lamellar system is absent, forms in the non-flowing blood. In microscopic structure this thrombus resembles a post-mortem clot, being made of an irregular admixture of red and white blood cells, blood platelets and fibrin.

The Cause of the Development of a Platelet Thrombus.—If we compare the blood stream to a river in which foreign particles are distributed, the conclusion would be warranted that any local heaping up of particles can only take place under an optimum special rate of flow. And so, in the blood stream we must presuppose that a certain diminution in the rapidity of the flow must take place to furnish the optimum condition. Thus in the stream in which barriers or dams are erected and changes in rate of flow are produced, deposits have been observed. So therefore, we would expect that in the formation of autochthonous thrombi we should find certain alterations in the blood stream that bring about sudden flowing or refluxes, or vortices.

The causal factors in this type of thrombosis have been given as,

- A. Changes in the rapidity of the blood stream;
- B. Changes in the qualitative and quantitative state of the blood platelets;
- C. Changes in the inner walls of the vessels.

A. Changes in the Rapidity of the Blood Stream.—The predilection of the venous system to thrombosis is in keeping with the possibilities of impediments to the normal rapidity of flow in them. In the venous system there are indeed sites of predilection, namely, the veins of the leg, the proximal portion of the femoral vein, the pelvic veins, the veins of the meninges, etc. Four factors contribute to the localization of venous thrombosis; (1) the continuous pressure on the venous wall—as is exemplified by the constant pressure of the column of blood in the veins of the lower extremities in the upright posture (or the action of intra-abdominal pressure in causing dilatation of the veins); (2) the ampullary dilatation of veins in the valvular pockets; (3) the possibility of reflux in the stream, first occurring in the proximal valves of the femoral veins; and (4) the resistance to flow that Poupert's ligament offers to the current of the femoral veins in the recumbent posture. The position of the patient is not unimportant in determining thrombosis in veins, for an extremity that is constantly held under another one is more apt to show complicating thrombosis. The compression of the left iliac vein through the iliac artery is not to be disregarded in its effect in impeding flow in the veins and leading to left-sided crural thrombosis.

B. Changes in the Platelets.—Whilst retardation of the flow is an important factor in the production of thrombi, the accumulation of platelets may be influenced otherwise. These thrombi have been variously called separation or accumulation thrombi (*Abscheidung und Anhäufung*). These terms have been applied because of the fact that the platelets are more or less intimately agglutinated. And so, in the literature, we find besides the appellation "*accumulation*," also the words "*conglutination*" and "*agglutination*" descriptively used in this connection. Here we presuppose an alteration in the viscosity of the platelets. We do not know, however, whether increased coagulability of the plasma also determines a more rapid agglutination of the platelets. Variations in the fibrinogen content may have some influence. Increase in the fibrinogen content alone *per se* does not lead to thrombosis, so that a direct causal relationship cannot be accepted in the present state of our knowledge.

Certain it is, that in artificial anemia, the platelets become markedly increased in number, and from this we may draw as a corollary the noteworthy observation that persons

¹ Aschoff, *Loc. cit.*

rendered anaemic by operation or gynecologic or obstetrical conditions show an increased tendency to thrombus formation.

C. Changes in the Vessel Wall.—The rôle of alterations of the intima in the production of thrombosis has been much overestimated. It is a well-known fact that the *atherosclerotic aorta, and other large arteries in spite of very intensive intimal changes, may be free of all thrombus formation.* It has been asked as to whether thrombosis can only occur when the intima has been damaged; chronic changes in the intima of the vein alone do not play a determining rôle in causing thrombosis. Where, however, there is advanced phlebosclerosis with rigidity of the vein walls and valves, with consequent circulatory impairment, we may conclude that a causal relationship exists. When, however, the intima is suddenly robbed of its endothelium covering, a pathological reaction of the tissues is necessarily unavoidable. In such a case it is the alteration in the territory of the wound that causes the thrombosis.

Coagulation in the Process of Thrombosis.—The observation (Baumgarten) to the effect that fluid blood does not clot in a section of a vessel that has been ligated in two places, would at first sight offer insurmountable difficulties to any explanations of the clotting process.

Aschoff says that the breaking down of platelets sets free fibrin ferments that admix with the surrounding plasma, and by a process of diffusion pass in a peripheral direction where the effects can be manifested. In the origin, therefore, of *red thrombi*, we presuppose not the separation of corporal elements of the blood (as in the platelet thrombi), but notably the throwing out of fibrin (as in the ordinary clotting process). And so the red clot (coagulation thrombus) is to be differentiated from the platelet (segregation or conglutination) thrombus. Some authors distinguish between conglutination or agglutination, and accumulation thrombosis and coagulation thrombosis. Whilst in the segregation (conglutination) type of thrombosis, the slowing of the blood stream and the quantitative and qualitative conditions of the platelets and their viscosity are the essential factors, so, in the case of the coagulation (red) thrombosis, the cessation of the stream and the ferment elaboration are essential.

It is evident, then, that one type of thrombus (the platelet thrombus) leads directly to the other type, the coagulation thrombus. Similarly we see in thrombo-angiitis obliterans a specific type of clot doubtlessly of inflammatory nature, directly associated with a coagulation clot that caps the terminal portion of the former (Chap. LXI).

Primary Coagulation Thrombosis.—It is a difficult matter to produce a primary coagulation thrombosis experimentally. Cessation of the blood flow alone does not suffice when the ferment development is not adequate. Indeed, optimum conditions, with a proper relationship between rapidity of flow and quantity of ferment are necessary to bring about the result. For, if ferment is present in large enough quantities, even the flowing blood may clot.

In some of the experimentally produced clots we may be dealing either with fibrin coagulation or what is known as "precipitation thrombosis." Two other factors, however, are known to bring about coagulation thrombosis. These are ligation and infection.

When the fibrin ferment that originates in an injured vessel wall through ligation can adequately exert its influence on the continuous non-flowing blood column, coagulation thrombosis may occur. The platelet thrombosis may also develop where the dead portion of the vessel is in contact with the blood stream. Both forms of thrombosis are possible, whilst with very slight injury to the wall neither one of these may follow.

In the so-called *infectious type* of thrombosis, the thrombus formation may *precede* the infection or be *caused* by the infection. In the puerperal thrombosis, and in post-operative infectious thrombus formation, by virtue of the

liberation of fibrin ferment, coagulation thrombosis may occur in numerous veins, and where the blood flow is interfered with, the platelet thrombosis may develop. If infection (particularly streptococci) be superadded, an inflammatory reaction within the vessel wall with the migration of leukocytic elements from the periphery into the vein wall, is to be expected. Puerperal cases often evidence a puriform condition within the veins, with marked periphlebitis, the picture simulating abscess rather than infectious thrombosis. In such cases the infection travels through the vascular walls rather than by way of their lumina.

The thrombosis that occurs in direct association with an inflammatory area is a complicated process. At first the venous tributaries become the seat of thrombosis, probably of the coagulation type, by virtue of the liberation of the fibrin ferment in the inflammatory toxic process. Then secondary invasion of bacteria takes place, and finally the larger veins, by reason of interference of the circulation, become the seat of platelet thrombosis. It is difficult to differentiate accurately in all cases between thrombosis as the result of an infection, or a thrombus secondarily infected.

Metastatic (?) or Distant Thrombosis.—It is possible to explain distant thromboses in three ways: (1) the microorganisms in the blood cause a local change in the wall of the vessel with secondary thrombosis; or (2) that in some unknown way, coagulation phenomena are brought about in the blood by the organism; and (3) that the primary thrombosis is independent of the infection, the manifestations of thrombophlebitis being produced by secondary invasion of the clots with the organisms.

(1) Metastatic inflammatory changes in the wall are clinically rare, but may possibly explain the occurrence of tubercular and syphilitic thrombophlebitides.

(2) Direct coagulation through the action of the circulating organism is only a hypothetical explanation, since experimentally such action of bacteria could only be produced when stasis in the blood stream is an added factor.

(3) Primary thrombosis with secondary infection is the most common type. In the femoral vein where thromboses so frequently occur in post-operative cases, the thrombosis according to Aschoff, was found to be of the platelet type. Distant thrombosis in the iliac veins occurs with no direct connection between the site of operation and the site of the thrombosis. Here, too, platelet thrombosis is the rule and when infectious thrombi are found, these show the bacteria in the platelet masses. The thrombosis, therefore, just as in the non-infected cases is the result of local alterations in the stream, and not the immediate result of infection, the bacteria invading secondarily. Then, as the bacteria multiply, degeneration of the thrombus elements takes place, and infiltration of the vessel wall with leukocytes follows. Superadded to such a thrombus there may be a secondary thrombosis extending centrally.

Thrombosis in Thrombo-angiitis Obliterans.—How are we to explain this variety of thrombosis, one that is exquisitely of the red variety, but in which three different forms are in evidence? The pathology of this form will be described in detail elsewhere. Here, for clarity it may be well to anticipate by stating that a red (or mixed) form is the immediate sequence of lesions in arteries and veins, whose walls have become the seat of an acute inflammatory process. Stasis probably plays a rôle, for only in this way can we explain the predilection of the vessels of the lower extremities for this disease. Secondary changes occur in the clot by the transmigration of corpuscular elements through the walls of the vessels. A "specific" architectural picture is thus evolved that seems in the light of our present knowledge to be pathognomonic. The latter changes are reactive, resorptive, and (teleologically speaking) paradoxically curative and baneful in nature.

The characteristic form of clotting could, in the interpretive system of Aschoff, be regarded as of the type due to "metastatic inflammatory changes in the vessel walls," although a specific organism has eluded the search of investigators. So also, could the process be included in the above-mentioned third category. For, the inflammatory and abscess-like foci in the clot might be regarded as indicative of secondary infection.

A bland, red form of thrombus within normal vessel walls, and evidencing no inflammatory and none of the specific reactive and resorptive phenomena is often found as a sort of cap surmounting the typical variety (accretion or stagnation thrombus). This, it would seem, is due to local cessation of the stream, possibly aided by the liberation of fibrin ferments.

The third form includes only the intermediate and final products of the first type.

Precipitation Thrombosis.—This is another form of thrombosis that has a rather theoretical than experimental interest. It may be described as that form in which thrombi result from the action of chemicals precipitating albumin. Whenever mucous membrane is cauterized chemically, such thrombi develop in the smallest veins; so also, when a heterologous serum or a specific precipitating serum is introduced into the veins. This phenomenon belongs to the type known as agglutination, the agglutinating red blood cells playing an important rôle. In the thrombi resulting from the action of poisons (ricin, adrin, snake venom), the clotting is partly due to agglutination phenomena, and partly to the obstruction of the smallest vessel with broken-down red blood cells. The effect of burns is a similar one. Aschoff has designated the type with breaking down of red blood cells as spodogenic thrombosis.

CLASSIFICATION OF THE THROMBOTIC PROCESS¹

According to form	According to causal genesis	
	Immediate causes	Remote causes
1. Segregation (separation or conglutination thrombosis).	Local retardation of the stream. Quantitative and qualitative alterations in the platelet.	(a) Physiological narrowing or dilatation. .phys. dilatation thrombosis. (b) Dilatation with pathological changes in the walls.pathological dilatation (c) Static factors.static thrombosis (d) Compression..compression thrombosis. (e) Vessel injury..traumatic thrombosis. (f) General weakness of the vascular system.marantic thrombosis. (g) Alterations in the blood. blood deterioration thrombosis. (h) Inflammatory wall changes. inflammatory thrombosis.
2. Coagulation thrombosis (clotting).	Local cessation of the the stream. Fibrin ferment.	Ligation Placental } Stagnation thrombosis. detachment Inflammation.Inflammatory thrombosis.
3. Clumping thrombosis (erythrocytic agglutination).	Agglutination of the red blood cells through blood poisons.Toxic thrombosis.
4. Precipitation thrombosis.	Albumin precipitation through caustic chemicals.	
5. Spodogenic thrombosis.	Breaking down of red corpuscles through blood poisons.	

¹ Aschoff, L, Beitr. z. Thrombosefrage, Leipzig, 1912.

Ribbert¹ differs in his conception of thrombosis from the views above expressed in that he believes that the platelet structure is a secondary formation after platelets have become adherent to an injured intima. When there is a small circumscribed lesion of the intima

¹ Ribbert, Virchow's Arch., 220, 1915, p. 133-147.

(experimentally produced) a small rounded mound of platelets covering the area is noted. An intimate relationship is always seen between the injured area and the platelet deposit. According to his view a retardation of the blood current, although it favors the adhesion of platelets, is not the determining factor, but the very beginnings of platelet deposit permit of continued deposition including also leukocytes and fibrin. In this way lamellae perpendicular to the blood stream originate. Where there is a "system" of platelet framework, Ribbert presupposes the existence of numerous platelet mounds, each giving rise to its platelet beam.

CHAPTER XIX

MECHANICAL TYPES OF THROMBOSIS

For a better understanding of the origin of thrombi within the body, a brief resumé of results of experimental work and of observation on effects of intravascular physical phenomena may elucidate the subject. In the following exposition the work of Beneke,¹ Lubarsch, Zahn and others has been extensively drawn up.

The deleterious influences can set in acutely or slowly, or may take the form of a variation in the character of the stream of flow. The former of these constitutes *stagnation thrombosis*, the latter the *pulsion*² thrombosis. The former of these corresponds to a certain extent to the coagulation type of thrombosis, the latter with the accumulation or seggregation type.

Stagnation Type of Thrombosis.—Experimentally, it has been shown that blood contained between two ligatures in a living vessel with uninjured vessel walls, will remain fluid. But such a section of vessel when cut out of the body and exposed to ferments, or when tissue extracts are injected (coagulins), undergoes early coagulation. In such stagnant blood, coagulation does not take place until by virtue of marked injury of the vessel wall at the site of ligation, or through chemical lesion of the wall and thermic influence, localized special causal moments have become established.

In territories undergoing stasis, increasing degeneration of the vessel wall is believed to take place by reason of inadequate gaseous interchange, with resulting breaking-down of the blood corpuscles. Their hemoglobin-free detritus may then fill the lumina, or lead to hyalin thrombosis. Then fibrin ferment develops, resulting in coagulation in spite of the inhibiting influences of the vessel walls.

In short, experiments seem to warrant the conclusion that true thrombosis results only then in stagnant blood when added mechanical thermic or toxic influences play a rôle.

Pulsion Thrombosis.—In this group we presuppose that through special modalities of flow, the normal mixture or distribution of the corporal blood elements is disturbed with a tendency to local aggregation of special groups or types, particularly of blood platelets. In this way agglutination, coagulation and congelation leading to plugs or thrombus formation are favored. Essential for such modifications are principally an abnormally strong development of the plasmatic marginal stream. These currents can be observed in flowing blood at the vessel wall, and they form the peripheral zone in which erythrocytes are absent. The physiologic significance of this territory is the constant reciprocal exchange of chemical relations between the blood and the vessel endothelium. Through this exchange the plasmatic marginal current is doubtlessly influenced. The rolling motion of the leukocytes independent of the axial current is believed to be partly due to the osmotic processes that are an expression of the secretory activities of the mural vascular elements.

For an understanding of the mechanical forces the excellent description of Beneke will be extensively used.

According to general hydro-dynamic laws the forte of the axial current (in a non-living tube) is the strongest and diminishes in intensity towards the wall of the tube. Theoretically there is a thin resting layer directly against the wall. The rapidity and breadth of the marginal current depend upon the energy and form of the total stream. A rapidly

¹ Beneke, Krehl-Marchand Handb. d. allg. Path.

² Terms used by some of the Continental writers.



FIG. 34.—Schematic representation of increasing size of marginal zone with diminution of pressure. (*Beneke*)



FIG. 35.—Schematic representation—changes in marginal zone at points of local dilatation. (*Beneke*)



FIG. 36.—Schematic representation—formation of whirls or eddies in vessels by reason of abrupt changes in the character of the lumen. (*Beneke*)

flowing axial current develops considerable natural pressure, and the marginal current can become insignificant; the less the lateral pressure, the broader the slow marginal zones may become.

In Fig. 34 the dark central area to the left represents a strong rapidly flowing stream that develops an increasingly broader marginal zone at *a*, where its diminishing intensity is also expressed by lighter shadings.



FIG. 37.—Schematic representation—the effect of dam-like obstructions (*a*) here depicted (*Beneke*)

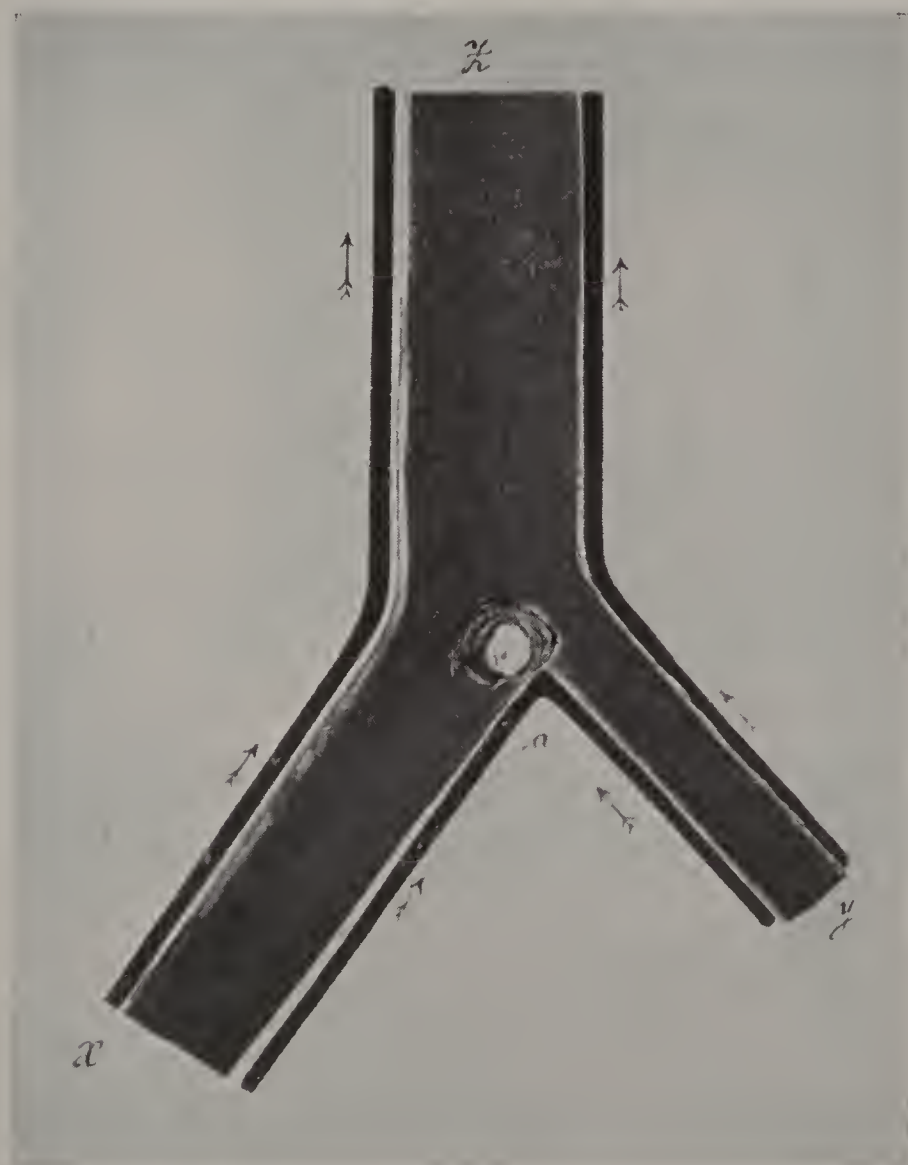


FIG. 38.—Schematic representation—formation of whirlpool where two marginal currents (*x-y*) meet at *a*. (*Beneke*)

Local dilatation (Fig. 35 at *a*) and general dilatation at (*b*) are accompanied by similar changes in the marginal zones.

Abrupt changes in a tube or vessel wall with generalized or local changes in diameter of the lumina (Fig. 36) may cause the formation of whirls or eddies or vortices. The propelling force of the stream current perpetuates these eddies, whilst any contained particles at the periphery of the eddies are cast off tangentially.

Narrowings in the stream through projections from the walls cause quite different phenomena. In Fig. 37 it will be seen that the upper portion of the stream conserves its strength, whilst the lower is altered through the presence of the dam-like obstruction at *a*. Behind the dam, condensation and attenuation of the axial current are produced together with waves. The altitude of these waves diminishes as they recede from the obstacle, varying according to the strength of the axial stream, their length being related to the height of the obstruction. Beyond the obstacle an eddy is formed that tends to flow in a everse direction.

It will be noted that just beyond the dam (to the right at *a*) there is a space, and then follows the eddy. The course of this eddy or whirlpool has been shown to be so great that solid particles in an experimental stream are thrown backward against the stream into the dead space. A correct understanding of these phenomena will enable the reader to properly interpret the theories of Aschoff.

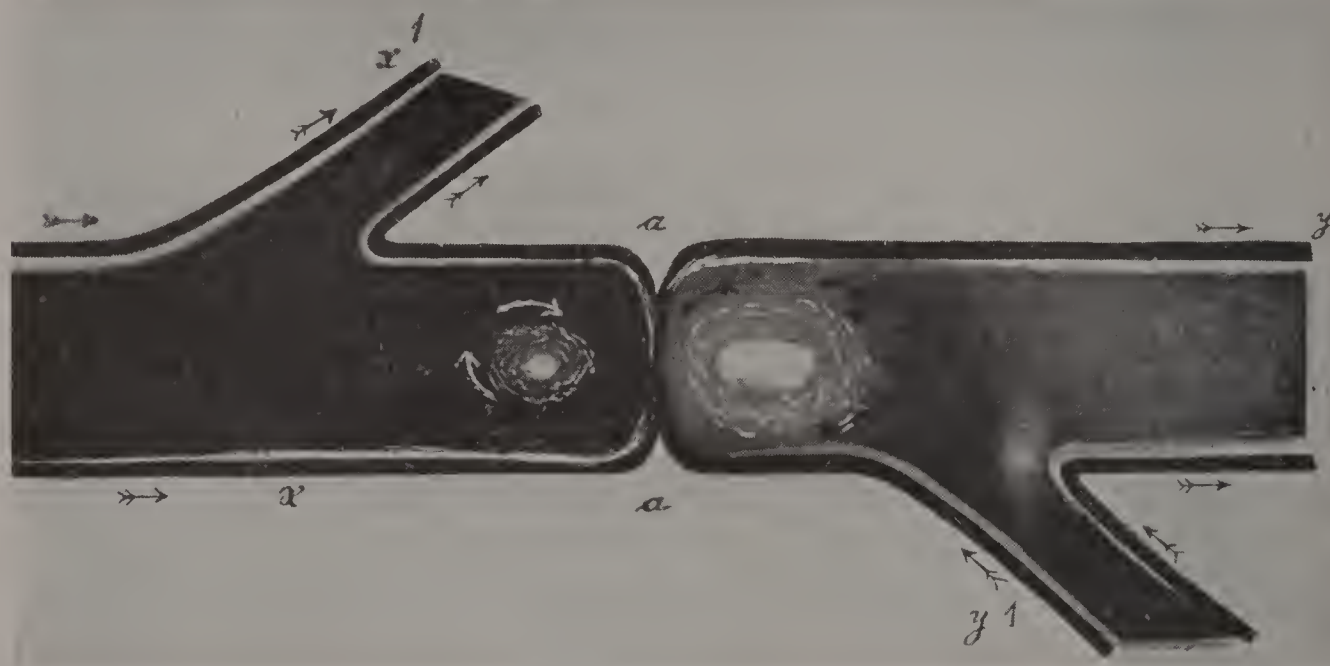


FIG. 39.—Schematic representation—the effect of ligation seen in the formation of whirlpools at the closed vessel ends. (Beneke)

Fig. 38 shows the development of a whirlpool where the two marginal currents of *x* and *y* meet at *a*. Whichever of the two streams is the stronger (let us suppose *y*) will displace the eddy into the lumen of the other, into a point of rest (*a*). The stronger the pressure differences between the two streams, the greater the transference into the lumen of the weaker current.

The effect of *ligation* is depicted in Fig. 39 at *a*, with the current running in the direction of the arrow. The current flows with accustomed full rapidity through the branch (*x'*), and forms a whirlpool in the blind end. A collateral (*y'*) which leads from the distal vessel becomes the seat of a reverse current. In the blind end of this part of the eddy a larger eddy is formed.

According to Eberth-Schimmelbusch (Fig. 40) the marginal current of the blood contains normally only white blood cells, whilst the platelets are admixed with red blood cells in the axial stream. Simple diminution of the rapidity of the current is followed by a distinct increase in the parietal leukocytes. With further diminution in flow the blood platelets are cast into the marginal zone in increasing numbers until the latter occupy most of this region. Even with this phenomenon a true thrombus does not form, and with a change in the rapidity of the current, these corporal elements can be again withdrawn into the central portion of the stream.

According to mechanical laws, the heavier red blood cells must follow the axial current, and according to the law of centrifugal motion must move in the periphery of the eddies. The marginal zone, as also the center of the eddies, must therefore under favorable circumstances contain mostly leukocytes and platelets. The breadth of the marginal zone, as also the extent of the whirlpool centers decrease with the intensity of the lateral pressure in the channel. Increased pressure tends to force the corpuscular particles into the eddy, against the latter's centrifugal tension. *Per contra*, when there is little pressure the eddy tends to broaden and the steadier elements can be more easily precipitated externally, and

the separation of specifically lighter articles from the heavier is favored. Since the eddy becomes broader with diminution in rapidity of the stream, the number of platelets and leukocytes increases with weak current.

Solid plugs develop experimentally with mechanical vascular lesions. When acupuncture is used in experimentation, all the blood corpuscles are pressed against the injured area, and then become converted under pressure into a hyalin stagnation thrombus. Where circulation is still present with waves and eddies, leukocytes and platelets coalesce. The latter agglutinate and form the beginnings of true thrombi. Where the current is very rapid, the thrombi may be absent, because the platelets are torn away soon after attachment. Changes in direction and weakness in the current are important factors in the formation of thrombi in experimentation.

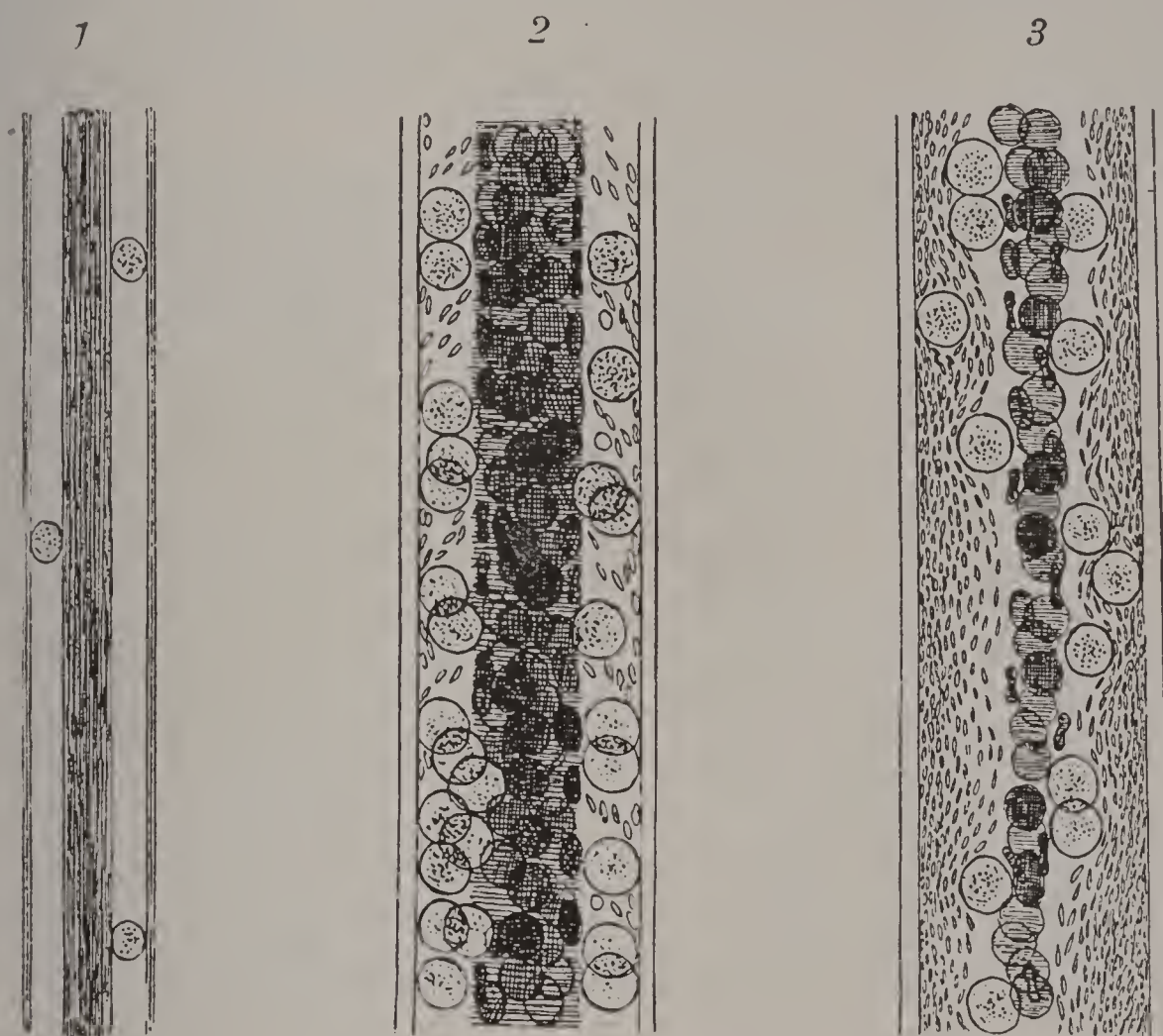


FIG. 40.—(1) Normal circulation showing central axial current and plasmatic marginal zone with discrete leukocytes.

(2) Circulation of diminished rapidity, the red blood cells visible in the axial current, accumulation of leukocytes at the parietes and beginning mural attraction of the platelets.

(3) Markedly slow circulation, marginal accumulation of platelets and leukocytes with sluggish, narrowed axial current. (Eberth-Schimmelbusch)

It has been shown, however, that although trauma is an important predisposing factor in thrombus formation, pure *mechanical agglutination up to complete thrombus formation can occur, as the result of changes in the current alone.*

In addition to the mechanical factors, *chemical influences* have been thought to explain thrombosis. Indeed, the experiments with hirudin seem to show that venous tears after hirudin or pepton injection are followed by typical platelet thrombosis, usually without fibrin, in inverse proportion to the amount of anti-coagulin injected.

When *foreign bodies* are introduced into the circulation, agglutinated platelets accumulate in thrombus-like formation over the foreign body in very few minutes. About such bodies, eddies and waves develop that lead to agglutination of the platelet elements.

That chemical influences must be taken into consideration, however, is demonstrated by the fact that foreign bodies covered with paraffin do not show such platelet agglutination. Perhaps in the case of foreign bodies, just as in the traumatic thrombi, the death of isolated leukocytes and platelets adherent to the foreign body evokes the incipience of further agglutination and attachment of the mechanically concentrated platelet masses. Platelets occur in places in which the current is relatively retarded.

In the *ligated vessel*, whirlpools of varying size and density are occasioned by the current. Usually with adequate collateral and intensive circulation thrombosis does not occur, since small agglutinates are easily detached by the current. In the presence of weak currents, however, thrombus formation occurs with growth of the latter into the free lumen of the vessel without contact with the walls.

But the retardation of the stream alone after ligation of a vessel does not seem to be the only factor in thrombosis. It must be conceded that at the present state of our knowledge it has not been possible to simulate the marantic thrombi in an experimental way. Some other chemical constituent of the blood must be sought for, which in the presence of mechanical contributing factors suffices to bring about thrombosis. Lipoid substances are believed to be not unimportant in this connection.

Stagnation Thrombosis.—Some observations would seem to indicate that thrombosis does not normally occur in a stagnant flow. The fact that it is absent in the umbilical artery after ligation of the cord is cited as an argument against the mechanical theory; and also the fact that vessels in the case of atherosclerotic closure of the crural arteries do not necessarily become closed by thrombi.

The instances where plugs do occur, however, in these circumstances cannot be ignored. Here possibly an additional factor besides the stagnation, either a change in the vessel wall or of the contents, is responsible.

In the case of the capillaries and small vessels, stasis contributes a certain essential condition, be it through simple mechanical interference to the outflow with a continuous inflow, or be it through the chemical changes in the tissues and vessels that are thus engendered. The phenomenon of stagnation does not seem to be the only effect of retarded circulation. In addition to the diapedesis and capillary dilatation, the erythrocytes are massed together and compressed, so that a homogenous fusing can take place. Then hemolysis, through the influence of mechanical or chemical injury to the endothelium may take place, the hemoglobin of the red blood cells may disappear, and their stromata left as a colorless, dense reticulum. In such agglutinates, platelets and leukocytes then degenerate and form foci for the production of fibrin clots. Such stagnant blood columns in small vessels and capillaries then have as a characteristic the rapid degeneration of all the cells implicated, and are thus differentiated from the stagnant blood in the cadaver.

The compression of the erythrocytes and the necrosing influence of slowly flowing but stagnant blood with the concomitant degeneration of other cells, particularly endothelial cells, seem to be the essential factors in the genesis of stasis thrombosis. In this sense *mechanical and chemical moments combine to produce the end-results.*

Red or mixed hyaline thrombi correspond to stagnation of the total blood. But colorless hyaline thrombi can develop in capillaries and small vessels without admixture of erythrocytes when tissue is injured, either through cold or long continued ischemia. In such case the residual leukocytes, the fibrin masses, and the transuded substances then form a hyaline substratum which is not unlike a hyaline urinary cast in form and genesis. Simple ischemia, even when of considerable duration does not cause thrombosis. In the local asphyxia of the fingers occurring after exposure in susceptible individuals, the vitality of the blood and tissues remains intact, only the flow is retarded. After excessive cold, there may be simultaneous death of the surrounding tissues as well as of the blood in the vessels, so that no vital exchange is possible; then, too, thrombosis is absent. Thrombosis takes place only when the remaining living tissues can exert their effects.

As compared with the stagnation thrombi in the smaller vessels, those in the *larger ones* are not essentially different, except that the separation of the colorless elements is not so complete as to produce obturation with these alone. In larger vessels one occasionally sees gross clotting of blood, not unlike cruor, following sudden interruption of the circulation (as in ligation of the plexus pampini formis). A sudden cessation of the blood flow results. However, even in the larger vessels such red thrombosis is usually under the influence of undulating currents, as manifested by the grouping of platelets and leukocytes, within the coagula. These form smaller and larger conglomerates that are evidences of the effects of the current's waves.

It is believed that there is always a necessity for a certain quantity of ferment for the development of red stagnation thrombi in the large vessels. Simple compression or even invasion of a vessel with an obturating tumor mass may not produce thrombosis.

Further observations speak for the immediate importance and relationship of local increase in ferments in the formation of stagnation thrombi. A primary thrombus as soon as it becomes obturating, may bring about a secondary red thrombus. This is also noticeable in the specific type of thrombi in thrombi-angiitis obliterans where secondary thrombi of red type are apt to cap the terminations of the specific clot. By reason of the action of the ferments, these secondary clots may extend for varying distances into the vessels and even into their branches. The extent of the secondary red thrombi exceeds the primary pulsion thrombus. Appearances of the secondary clot, too, speak for the

diminution in the amount of ferment as the clot recedes from its point of origin. Where the secondary coagulum is attached to the primary thrombus, it is firmly connected, whilst farther away it tapers out and gradually shows an imperceptible transition into the fluid blood.

In short, the origin of red stagnation thrombi is traceable to two principal factors—firstly, a weakening or deficiency in circulation and secondly, the presence of substances in loco that further fibrin clotting.

Pulsion Thrombosis.—This is the most frequent form of human thrombosis, and was first given complete study by Zahn,¹ who called attention to the relationship between the wave motion transmitted in the pulse and the conformation of thrombi. Virchow, von Recklinghausen and Zahn, therefore, were the founders of the mechanical theory. They conceived that retarded flow, whirlpool or eddy formation and undulatory movements were possible factors in thrombus formation. The participation of blood platelets as important components of white thrombi was first called attention to by Osler²

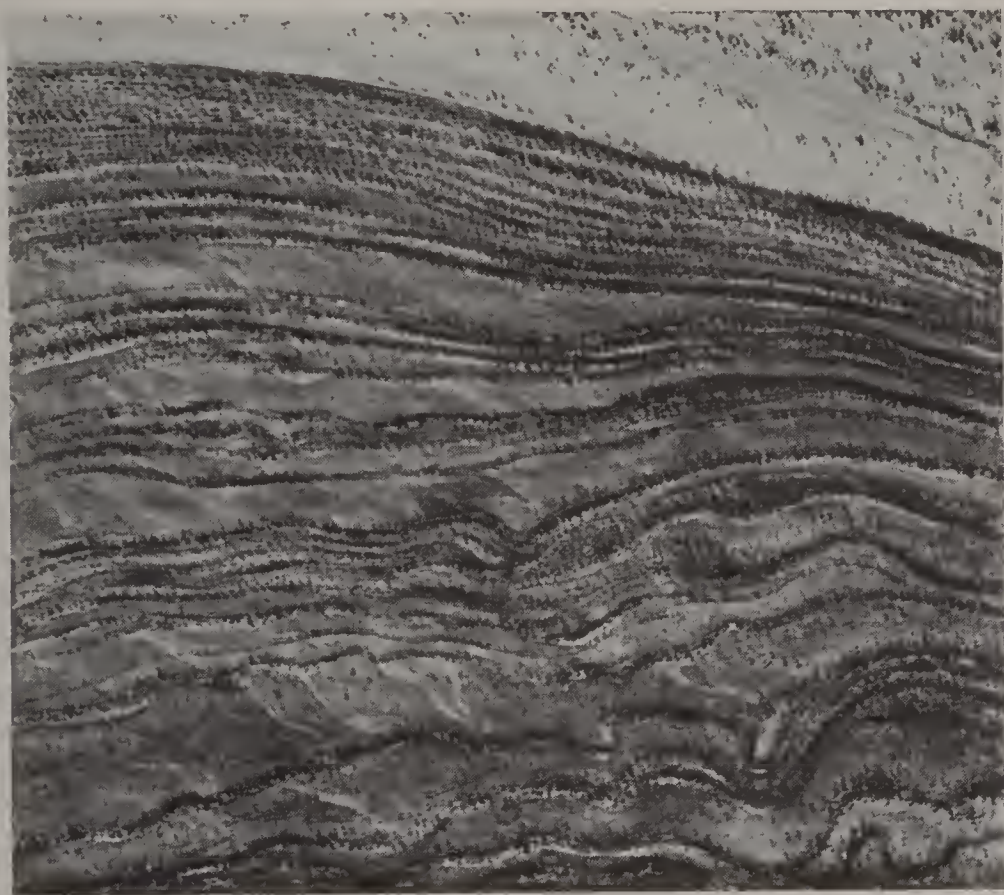


FIG. 41.—Schematic representation of stratified formation of thrombi reproducing the wave currents. (Beneke)

and Hayem.³ Pure platelet thrombi are not common in the human organism. They occur only there where the platelets can stick together and form firm masses, whilst the deposition of leukocytes and fibrin is prevented by the current. These conditions obtain where there is a strong current, particularly in arterial territories, as for instance, over areas of aortic sclerosis, aneurism, etc. In the venous channels leukocytes can become attached by reason of the diminished flow and agglutinate. Platelet thrombi are very often seen in the furrows in the arterial walls over atheromatous ulcers. Thereupon the blood stream may model such thrombi. They cover the arterial wall with protecting hyaline covering and later may become calcified.

White thrombi made up of platelets and leukocytes, with or without fibrin, are more common than the pure platelet thrombi. They begin with the deposition of the platelets; then occurs the attachment of leukocytes and fibrin.

The most important forms are the wave and whirlpool or eddy thrombi. The agglutinated cells lie in the nodal points of the waves and in the centers of the eddies. According to the intensity of the blood stream they may be dense and narrow, or they may be loose and broad.

The deposition of fibrin then follows by reason of the participation of the degenerate leukocytes. The agglutinates forming in the retarded stream lie in the nodal points of the

¹ Zahn, Virchow's Arch., LXII, 1875; also XCVI, 1884, and CII, 1885.

² Osler, Ztschr., f. med. Wissensch., 1882.

³ Hayem, Recherches sur l'anat. norm. et path. du sang, 1878.

waves and in the centers of the whirls. Even the very smallest agglutinates show deposits of leukocytes. All the various degeneration forms can be seen, namely, detached granules of platelets, karyorrhexis, breaking down of the nuclear substance—are noted. Because of the large number of leukocytes one gains the impression that chemotactic influences attract them. The participation of leukocytes is of importance for the growth of the white thrombi in typical formations, in which a central agglutinate free from nuclei forms, and about which there is a zone of leukocytes. The breaking down of leukocytes goes hand in hand with the deposition of tissue material.

Fibrin formation follows the chemical participation of degenerating leukocytes, beginning from the degenerating center. Fibrin threads surround the centers, and attain their greatest size between two coagulating centers. Histologic pictures are often observed which correspond accurately to the wave conditions present. Thus one finds at intervals more or less oblique masses of thrombus made up of platelets and leukocytes corresponding to the nodal points. Between these one finds the fibrin threads like water plants taking the direction of the stream, and whose obliquity and curve depend upon the strength of the lateral pressure of the current. Lamella formation is another product of the mechanical hydrostatic conditions. The parallel formations are due to repeatedly new depositions in the nodal points in a direction perpendicular to the current. This forms the reef-like surface of thrombi being a replica of the wave current (Fig. 41).

The erythrocytes only play a subsidiary rôle in the process. When they are included between the layers of fibrin, they may persist for a long time without degenerating. They may be absent between the layers, as in the case of the white thrombi, which arise in the plasmatic part of the stream. Only then when the strength of the stream becomes so diminished that the peripheral portions of it are stagnant, and the erythrocytes also taken up in the wave thrombus, just as in the stagnation thrombus, then are produced those peculiar mixtures of red and white layers or mixed stratified thrombus (Fig. 41).

In the *mechanically* produced thrombi the process sets in through agglutination of the platelets and the secondary fibrin formation and leukocytic accumulation that results from the autolytic poison. Therefore, to a certain extent even the mechanical thrombi are of chemical origin. The active substances causing the thrombosis emanate from the midst of the stream and from the constituent elements of the blood aided by the absence of inhibiting influences. The inhibiting influences under normal conditions are the constant dilution of the toxic substances in a normal blood current, and the checking action of the vessel wall, both of which are disturbed when mechanical influences are at work.

CHAPTER XX

THROMBOSIS OF CHEMICAL ORIGIN

By true chemical thrombosis we designate those forms in which the plug formation arises by reason of chemical influences that penetrate from without through the vessel wall, or that are carried by the blood. Several varieties of thrombi are thus formed, the so-called *spodogenic thrombi* due to precipitation, and fibrin forming or agglutinating types. Fluid substances diffuse rapidly in the blood and have a general effect; more solid substances, by reason of their concentration, act locally and mechanically on the blood and vessel wall.

Amongst chemical influences are included fluid and solid chemical agents, effects of general blood intoxication (from endogenic and exogenic poison), with injury of the vessel wall, and also thermic and actinic factors.

Substances injected into the veins experimentally for the production of thrombosis, naturally exert their effect upon all the blood elements, although they may specifically alter certain elements more than others, particularly the erythrocytes. Injection of ox blood serum into the veins of rabbits produces fatal agglutination in the lung vessels. Hirudin injection does not prevent such agglutination which indicates that this process is not a fibrin coagulation. Fibrin formation has been produced experimentally in dogs by the injection of foreign serum. Hirudin injection prevents death by inhibiting fibrin clotting.

Other forms of blood clotting have been experimentally produced through the injection of substances, that either destroy the blood corpuscles at once, or break them up (spodogenic thrombi), or that cause precipitation thrombi by granular deposition of the soluble albuminoid substances in the plasma (Dietrich¹). Von Bardeleben² found that even rich cultures of streptococci when introduced into the blood, did not cause thrombosis, but only when stasis was caused in a vein in which cocci were developed.

Dietrich, when he injected hemolytic agglutinating or precipitating substances into the blood stream, encountered typical seggregations or platelet thrombi whenever the blood stream was diminished in intensity.

The simultaneous injection of chemicals and injury to the vessel wall is especially effective through the latter agency. With complete necrosis of the vessel wall the hyaline and static type of thrombi develop (stagnation thrombi). More mild degrees of vessel injury cause thrombus formation corresponding to the pulsion type, insofar as they are derived from agglutinates of platelets and develop into white thrombi. The removal of the vital function of the endothelial cells alone leads to agglutination thrombosis, whilst simultaneously cooperation of fused toxic substances may lead to precipitation or to agglutination.

In the larger arteries the same insult (*e.g.* caustics) are not so apt to cause thrombosis as in the veins, in which agglutinates are more likely to adhere. The degree and the nature of the mural changes are important for the origin of thrombi. Whenever reaction is present in the walls, particularly with fibrin formation, the conditions for thrombus deposition are present. On the other hand, when the toxin diffuses, precipitates or agglutinates are more apt to form.

Inflammatory Processes.—Hyaline thrombi often accompany inflammatory processes, So long, however, as the inflammatory irritation of the vessel wall does not interfere with its vital functional capacity, thrombosis may be absent. Even accumulating leukocytes may not give rise to thrombosis, and it is not until these necrose and degenerate that thrombosis ensues. When, by virtue of specific action, fibrin deposition occurs in the lumen, then thrombosis immediately occurs.

In the larger vessel fibrin formation may occur within the vessel wall and layers. This may extend into the vessel lumen. Then thrombosis occurs. It is easily understood that inflammatory exudation of fibrin on the inner surface of the vessel wall would be relatively stronger when the current is slow, as in the veins. This is in accord with the more frequent combination of thrombosis with phlebitis than with arteritis. Talke³ was able to produce obturating thrombosis in the sheaths of vessels in which staphylococci were inoculated. The thrombi were probably evoked through the diffusing toxins, and the bacteria secondarily entered these clots. At first platelet deposits were noted by this author, and later, red or mixed clots.

In the case of staphylococci it has been found more difficult to produce such thrombosis, other factors being necessary such as marked retardation of the stream. Other authors were able to produce thrombi, with the injection of bacterium coli in the walls of the vessels.

In all of these experiments it is not the specific toxins of bacteria that predispose to thrombus deposition, but the total inflammatory exudate with its plasmatic, fibrinous and leukocytic accumulation, that evokes fibrin coagulation and platelet agglutination.

Chemical Varieties. Endogenous Poisons.—In extensive burns poisons are doubtlessly formed in large quantities, in contiguous tissues. Their absorption can be regarded as the cause of death. It has not been decided as to what rôle these poisons play in the production of thromboses in the organs. Thrombi, indeed are found in the form of hyaline masses in the small vessels and capillaries of the organs, particularly in the stomach and duodenum, sometimes associated with small peptic erosions. Aschoff reports small white thrombi in the lung arteries in a case. A thrombophilic tendency after burns, as an expression of the general intoxication, has not been proven.

In eclampsia there is a characteristic predisposition in certain organs to the formation of autochthonous capillary thrombi. Perhaps certain chemical local changes including degeneration of red and white blood cells in the liver, or the protagon and cholesterin contents in the brain, lungs and kidneys, are

¹ Dietrich, Path. Zentralbl., 1912, XXIII, 10.

² Von Bardeleben, Arch. f. Gynec., 1907, LXXXIII.

³ Talke, Beitr. z. klin. Chir., 1902, XXVI.

the factors that increase tendency to thrombosis. The increasing leukocytosis of pregnant women has been regarded as a morphological expression of a particular status of intoxication, perhaps of ferment production. On the other hand, it is well known that the coagulation time is not notably changed in pregnant women, nor is the cadaveric blood of eclamptics more prone to clot. It is believed, therefore, that whatever thrombosis occurs in such cases is rather due to an intensive local chemical action in which lipoid substances play a special rôle.

The occasional occurrence of sinus thromboses or similar implication of the lung arteries in children suffering from severe dysentery, has been explained on the supposition that there is absorption of poisons from the intestines. Circulatory weakness, however, is more important in these cases. Here, just as well as in the thrombi associated with carcinoma cachexia, it is found that the thrombi correspond in structure to the mechanical pulsion thrombi, and not to the experimental intoxication thrombi.

The so-called ferment intoxication can be brought into play through injection of defibrinated blood of the same species, through foreign blood, or special ferment solutions. It has been known for a long time that foreign blood as well as tissue extracts produced clots, a condition most apt to occur in the large blood vessels.

When tissue extracts are introduced into the circulation, sudden death from intravascular coagulation may result. An albuminoid substance, foreign to the blood, and not the precursor of thrombin, is believed to be found especially in the tissues.

Fibrin ferment in solution such as serum has been shown by Dienst to cause sudden death in rabbits through embolism of the lung with coagulation in the right heart. Small quantities produced very toxic injuries to the parenchyma of the kidney, up to necrosis with the formation of hyaline and platelet thrombi in the capillaries.

Exogenous poisons, such as ether, benzol, chloraform, pyrodin, ammonia, potassium chlorate, amyl nitrite, ricin, etc. have been known to bring about similar results. As for the influence of bacterial poisons—Loeb reports formation of red thrombi following injection of staphylococcus toxins.

The Action of Exogenous Poisons and Infectious Agents.—Changes in the total blood in the sense of increased coagulability are rare. Extensive cruor formation in most of the vessels is seen post-mortem after carbon monoxid poisoning. After transfusion of foreign blood lethal clotting has been observed. In eclampsia, anemic infarcts have been observed in the kidneys, due to hyaline thromboses with a picture of anuria. In the transfusion of foreign blood hemolytic processes leading to ferment over production and to local accumulation of erythrocytic fragments may occur. Thrombi of various types appear in the capillaries in various types of poisoning (bichloride and anilin).

All poisons that act in a destructive way upon the blood, do not necessarily lead to thrombosis. Thrombosis is absent in the cases of methhaemoglobinemia after potassium chloride and nitrite poisoning.

As a rule the larger parasites do not cause thrombosis when they are found in the blood. The trypanosomes, even in large numbers, do not lead to clotting. This is also the case with bacteria. Even when there are atheromatous ulcers, bacteria do not seem to further the deposition of clots.

The presence of bacteria does not essentially modify already existing mechanical thrombi, such as occur at points of ligation in the placenta. One would expect a favoring influence upon the growth of bacteria by reason of the presence of a clot, but indeed it is noted that bacteria are sometimes inhibited in their proliferation by just such a thrombotic process.

One may conclude, therefore, that infection with a variety of different bacteria does not suffice, as a rule, for the creation of thrombosis. Even in diseases such as fibrinous pneumonia in which conditions are present that lead to a saturation of the blood with fibrin ferment, thrombi are not so frequently

found as one would expect. When, however, bacteria such as streptococci invade the lumen of vessels in considerable number, fluid pus develops in veins very frequently without thrombosis. Sometimes such pus is separated from the current through a clot. Thus, we may conclude that the bacterial contents of the blood and bacterial poisons are not essential for the origin of thrombi in infection. Septic thrombosis is produced rather by disease of the vessel wall.

In atheroma Lubarsch does not consider the intima changes as playing an important part in thrombus formation. When the current is strong, thrombi rarely become attached to such patches. When there is mere fatty degeneration of the endothelium, thrombosis is usually absent. Even extensive change in the vessel wall, such as amyloid alterations of a large vessel or capillaries, does not necessarily lead to thrombosis. Chemical factors are however, important when smaller or larger vessels suffer necrosis through the action of poisons. Essential for thrombosis, therefore, would be the presence of diffusible poisons that enter the blood and modify it; or an active participation of an altered vessel wall through unusual special responses. In some cases the injury to the blood elements through the vessel wall is a chief factor; as following the injection of poisonous substances, or following the action of strong poisons through surface defects.

The form of thrombosis then varies according to the peculiar characteristics or qualities of the toxic substances. Thus, in the case of acid poisons entering through the stomach, such as sulphuric acid, a sort of stasis thrombosis occurs, with distension of the capillaries and smaller vessels with red thrombi. Or, in the case of putrid cystitis or pyelitis, hyaline thrombi occur in the neighborhood of ulcers and degenerate tissues.

In clinical pathology most interesting are the local vessel wall infections, particularly of the veins. A vein that is inflamed with staphylococci and streptococci shows the same leukocytic infiltration as any other tissue. With this a fibrinous excretion within the walls takes place. The process may be limited to the wall itself, particularly when only the adventitia is involved, the blood flowing within the vessel without being affected. When the fibrinous deposition is more diffuse, and enters the inner layers of the wall of the vessel, then platelet masses become attached to the intima. It is believed that the fibrin masses combine with the platelets, and can be traced to communicate directly with the intramural fibrin deposit. Most of the fibrin, however, has its origin in the flowing blood and does not emanate from the vessel wall. As the thrombus grows, it presents a mechanical obstacle to flowing blood, and there results the usual wave and eddy formation with corresponding mechanical accumulation of new thrombus masses.

Infectious processes vary in their influences on thrombus formation. Whilst thrombosis is seen in the superficial veins in syphilis during the precocious form of syphilitic migrating phlebitis, it may be absent in the umbilical veins, even though circulatory conditions are favorable for clotting. In the secondary stage, with endo- and periphlebitis syphilis does produce thrombosis (Hoffmann, Chap. LXXX). In tuberculosis extensive phlebitis migrans has been seen to occur without thrombus formation (Schwarz¹). Glassy masses are known to fill the veins in the neighborhood of severe diphtheritic lesions, an expression of the reaction of the circulating toxins.

The tubercle bacillus may develop nodules in the vascular wall (vessel wall), which may later give rise to mechanical thrombus deposition (Benda²). But, even here the thrombus

¹ Schwarz, Virchow's Arch., 1905, CLXXXII.

² Benda, Berl. klin. Wchnschr., 1908, XLV, 7.

formation is usually rather insignificantly organized. Parietal thrombi were seen in the case of Beneke where there were about a dozen such deposits in a number of veins of the lungs. They had the appearance of droplets that had become congealed as they flowed along the wall in a central direction.

In meningeal tuberculosis, however, the thrombi caused by fresh tubercles in the pia usually are obturating.

In the inflammatory diseases of the arteries, with the exception of thromboangiitis obliterans, thrombosis is not as common as would be expected. Inflammation of the vessel wall, as a rule, only produces thrombosis then in the large vessels, when mechanical deposition is facilitated through changes in contour, such as aneurismatic dilatation. A very striking type of thrombus formation is that of *periarteritis nodosa* (Chap. LXXIX) or polyarteritis. Here foci of intensive inflammation develop in the smaller vessels, leading to destruction of the vascular wall. As soon as the intima is reached, aneurismatic dilatations occur with thrombosis. Fibrin, leukocytes and hyaline masses occupy the clot. Destruction of the arterial walls furthers the thrombus formation. In the veins the circulatory sluggishness; in the arteries transitory vasoconstriction with consequent fibrinous deposits, are factors that predispose to thrombosis.

In the case of capillaries in an inflammatory area, leukocytes may clog their lumina and lead to the formation of hyaline masses. This occurs in pneumonia, in which glassy thrombi are characteristic.

Thrombosis Due to Solid Bodies.—Here we deal with the blockage of vessel lumina through migrated body constituents, with or without bacteria, as well as intravascular parasites.

In fat embolus there is but little tendency to thrombosis. In the neighborhood of fractures, the veins may contain fluid fat that is held fast by thrombi. Air (air embolus) does not incite clot formation.

Normal tissues have not identical chemical actions. We deal usually only with solitary cells (placental). These circulate and do not act in a deleterious fashion on the blood elements. When they die off, the injury produced is so minimal as to exert no thrombotic effect. Where larger fragments of tissue, such as pieces of liver, are mechanically displaced after liver traumata, the action is mechanical.

The displacement and the distant transportation of material containing ferment, such as detached thrombus particles, produce much more extensive additional thrombosis. Transported thrombi by reason of their ferment properties, predispose to further coagulation, and after death are even known to be the points of origin of fresh cruor masses. Very long secondary thrombi are often attached to such emboli, an evidence of their chemical action.

Thrombosis Due to Thermic Influences.—Thermic forces are exerted through injurious action on the blood itself, or through lesions of the vessel walls. Both heat and cold can produce thrombosis.

The general effect of extensive burns has been regarded as an expression of blood destruction due to ferment intoxication and attended with extensive blood coagulation. Other authors deny that extensive coagulation takes place. It is believed that large quantities of ferment are developed at the site of the burn, enter the blood and cause thrombosis.

The observations in the human conform to the experimental investigations. In the case of extensive burns the picture of intoxication preponderates over the thrombotic lesions.

Mild degrees of heat lead to hyaline thrombi in the affected locality. The clots fill the vessels, inflammatory reaction of the vessel wall being absent. Probably congelation of the dead leukocytes produces the plugs here. In the capillaries and small veins, at the margin between dead and healthy tissues, thrombi are not infrequently found. In some cases the clots have been regarded as precipitation phenomena.

Effects of Local Refrigeration.—The experiments of Zahn¹ showed that cold produces stasis and then thrombosis in the arteries, veins and capillaries. Experimental freezing in rabbits and guinea pigs demonstrated the development of typical inflammatory pictures. True thrombi do not necessarily form, but when the leukocytes attracted in this process, are caused to die off. Then these are converted into hyaline masses; and, together with the fibrin they fuse into masses that are regarded as thrombi. Even the vessel wall, when the action of cold is intensive, may participate in the degenerative process, become hyaline, and fuse, as it were, with the thrombus. In this way, extensive congelation thrombi may form in the region of the frozen area. In the necrotic areas themselves, the thrombi may be absent, being confined to the marginal zone between healthy and dead tissues.

The longer the cold effects are allowed to act upon the tissues, without direct necrosis, the more the circulation is impaired, and the more extensive the formation of hyaline thrombi. The circulatory conditions are determining factors in many cases. It has been shown that experimental section of the sympathetic nerve in the necks of rabbits was followed by more marked thrombosis than in those in which the vascular nerve mechanism was intact.

Thrombosis Due to Actinic Causes.—Electricity, X-ray and other actinic influences seem to exert about the same effect upon the blood and tissues as thermic insults. Local thrombi are caused by these whenever their action is sufficiently intensive to produce necrosis in blood or tissues. Jansen² describes local thromboses after light treatment; and Askanazy³ observed thrombosis after the use of ultra-violet rays.

CHAPTER XXI

GENERAL CAUSES OF THROMBOSIS

Thrombosis may depend (1) on factors inherent in general diseases; (2) on local mechanical or chemical alterations; and (3), on special conditions.

1. Thrombosis and General Diseases.—Beneke in his excellent work in this field proposed a grouping into general mechanical and chemical causes.

Cardiac weakness, whatever may be its origin, is an important factor. This may be brought about by toxic and infectious degeneration, excessive stress through stenosis, valvular insufficiency, or local disease of the cardiac muscle, as well as through senile change. In many of the post-operative thromboses and the marantic group, such conditions play a rôle. For, the clotting is most apt to take place where circulation is sluggish, as in the venous system, or where waves and vortices are likely to occur.

Local stasis, too, may be regarded as a contributing cause and with general circulatory weakness eventuates in thrombus formation. Indeed, Beneke states that ligation or tumor invasion of large veins need not give rise to this process until marked stasis occurs as the result of cardiac weakness.

Changes in the *character and form* of the stream, associated with currents interrupted by vortices and waves are important forces making for thrombosis. Examples are varices, aneurysms with variations in the size of the arterial lumen, sclerosis of the coronary,

¹ Zahn, *Loc. cit.*

² Jansen, Ziegler's Beitr., 1907, XLI.

³ Askanazy, Pathol. Anat., (L. Aschoff), Fischer, Bd. 1, 1919.

cerebral, and popliteal arteries. If a sudden alteration in the lumen is met by the flowing blood, eddies and vortices ensue, which with other agents such as cardiac weakness or special local muscular demands, may lead to thrombosis.

All these aforementioned factors are potent in proportion to the weakness of the general circulation. And so the preponderance of venous thrombi over the arterial is explained. Conversely, a strong current will inhibit thrombus formation.

Although the mechanical forces may suffice to generate thrombi, the latter may fail to develop where all the conditions for their production seem at hand. Hence qualitative and quantitative alterations in the blood corpuscle elements and their chemical relationship to the plasma, have been invoked in explanation. These possible motivating agents may be summarized as (1) anomalies of the blood cells including increase or diminution in the number of erythrocytes or platelets, leukocytosis and leukopenia; (2) anomalies of the plasma such as altered carbon dioxid, calcium ions, fibrinogen, fibrin ferment content; and (3) diverse conditions, such as increased agglutinability of the platelets, effects of age, cachexias and infection. All these may be of chemical nature.

Although it is often impossible to gauge the importance of chemical factors in a given case, the following brief summary may help clarify our interpretation of etiology.

The Alterations in Corpuscular Elements.—An increase in the number of erythrocytes seems to have no essential influence on thrombus formation. Polyglobuly or plethora may cause disassociation or separation of plates and thereby diminish the tendency to clot. A superadded factor, however, such as cardiac weakness, may nullify this and thrombosis nevertheless supervene.

A diminution in the number of red blood cells (erythropenia) may further the clotting process by an association of factors. Perhaps the diminution in the size of the vascular marginal zone in erythropenia may be a mechanically conducive element. To the coincident numerical increase of platelets must be also ascribed a certain rôle. So also, has been explained the mechanical thrombosis occurring in anemic persons. However, there is not a great tendency to thrombosis in anemic conditions, unless cardiac weakness is added as a factor.

In chlorosis, however, we have an exception, in that the inferior vena cava, the crural and renal veins are reported as being more than ordinarily predisposed to thrombosis.

Leukocytosis is a condition which theoretically would favor thrombus formation. Beneke believes that this could occur through deposition of leukocytes at any platelet center, and through the elaboration of ferments.¹ And so in leukemia the frequency of thrombosis has been especially noted (thrombosis of corpora cavernosa in priapism). Whether there is an overproduction of fibrin ferment, as has also been suggested by Dienst² in eclampsia, has not as yet been definitely proven. Leukopenia does not seem to influence thrombus formation.

Increase in the number of platelets has very frequently been recognized as conducive to a state of thrombophilia. Some of the post-operative thrombi occurring 4 to 5 days after a severe loss of blood, at a time when platelet production is most intensive, has been regarded as due to this phenomenon. It has not been satisfactorily proven, however, that a platelet increase *per se* is a cause of thrombosis. Diminution in the platelets, similarly, in severe anemias and acute febrile conditions does not explain tendency to thrombosis.

2. Chemical Alterations of the Total Blood.—The carbon dioxid content of the blood may inhibit coagulation by reason of the altered sensibility of the platelets, for these are said to degenerate through such chemical changes in the blood. In spite of this chemical restraining element, conditions in which there is increased carbon dioxide in the blood, such as stasis, show an increased tendency to thrombosis, due to the fact that the mechanical conducive moments more than counterbalance the chemical inhibitory.

The Ca- Ion content of the blood has been regarded by some authors as important in thrombus formation.

¹ See the case of Dr. G. in whom extensive obliteration of the vessels of the lower extremities, probably due to thrombosis had occurred, and in whom leukocytosis was present for many months and possibly years without known cause (Chap. LXXXII).

² Dienst, Archiv. f. Gyn., 1912, XCVI, 1.

The fibrinogen content, according to Welch and Aschoff is not responsible for altered susceptibility to thrombosis. Of more importance is the fibrin ferment content of the blood. Sudden increase of this element in experiments causes extensive clotting in the large vessels and immediate death. This lends confirmation to the view that excessive local ferment production may enhance thrombus formation. In the circulating blood neutralization or the destruction of ferments goes on constantly. The experiments of Dienst would indicate that in some cases sudden, in others a more or less continuous, overproduction of ferments may occur.

Cases are reported of extensive sudden thrombosis following small, minimal, primary, mechanical thrombi, and requiring but a very few minutes for their development. Two cases are cited in menstruating women. In one of these after a clean appendectomy, sudden coagulation of the blood in the inferior vena cava took place, resulting in pulmonary embolism and death within a few minutes, in the other case a red thrombus in the uterine veins seemed to be the starting point. In both of these, the authors concluded that there was sudden invasion of the blood with fibrin ferment, that enabled a very small mechanically produced thrombus to give rise to extensive coagulation. Mixed thrombus formation over a large territory has been reported in chronic nephritis where a more or less continuous state of increased ferment production was assumed to exist.

In the extremities we have not infrequently observed the association of extensive red thrombosis with emboli after infectious diseases and pneumonia. The sudden extension of thrombus formation throughout all the larger arteries and veins does not always occur in various embolic processes. Indeed, the absence of such secondary thromboses in most of the cases of arteriosclerotic blockage is noteworthy. The frequency thereof is striking in the above mentioned cases. Perhaps here, too, an overproduction of fibrin ferment, is a factor.

3. Special Conditions.—Little is known regarding the influence of increased *viscosity* as a factor in thrombosis. Increased viscosity of the blood is said to take place with increasing age,¹ and in certain infectious diseases (tuberculosis and pneumonia).

Welsh found no direct relation between coagulation time and viscosity.² Holmgren,³ however, takes the view that the polymorphs influence viscosity and the latter coagulation. His experiments tend rather to show a relationship between the polymorph content or polymorphlymphocyte quotient, than upon viscosity of the blood *per se*.

Except in the case of cholera, in which concentration of the blood follows the withdrawal of water, no particular tendency to mechanical thrombosis has been observed in conditions with increased viscosity.

The relation of thrombosis to *age*, has given rise to much speculation. The chemical differences in the blood and the quantitative relation of the platelets and the changes in the vessel wall have all been regarded as factors in the tendency of adults to thrombosis. That cardiac weakness may be a factor in the senile cases must be admitted. Nevertheless chemical alterations must not be lost sight of, and are probably of considerable importance.

In the thrombosis of *cachectic conditions* and in the marantic conditions, the quantity of blood and its composition, or the chemical relationship between the corporal and fluid elements have undergone change. Pathological

¹ Hess, Deutsch. Arch f. klin. Med., 1908, XCIV, 404.

² Welsh, Heart, Vol. III, 1, 1911.

³ Holmgren, Deutsch. med. Wchnschr., Jan. 30, 1913.

products of metabolism circulate in the blood, or the blood is depleted of certain substances. Malignant cells may have a special affinity and attraction for blood components.

In the present state of our knowledge we must admit the possibility of a chemical component in the production of the marantic thrombi. Only in this form is their dependency upon mechanical forces brought to our notice.

The Rôle of Infection in Thrombosis.—Infection can indeed play an important part in thrombosis. According to some authors this is due to an extensive vasculitis. Inflammatory foci with or without bacilli in the vessel wall, and the action of toxins have been regarded as the causes of parietal or other thrombi in typhoid fever. Systematic investigation of the occurrence of endophlebitic foci in the various infectious diseases has given rather negative results. The evidence seems to show that although focal infection of the walls of the vessel cannot be denied in infectious processes, no important rôle can be ascribed to these lesions in usual thrombus formation. The occlusive thrombosis in certain special types of phlebitis of unknown origin and in thrombo-angiitis is an exception (Chap. LXXXI). It would appear that the direct effect of bacteria and their toxins upon the total blood (or the forces engaged in circulation) are more important. The cardiac degeneration brought about by infection affords one of the mechanical conditions. So also, the existence of other coincident conducive agents cannot be denied.

Aschoff points out that embolic infarcts even in sepsis are not necessarily bacterial, but frequently agglutination thrombi with secondary invasion of organisms. Up to the present time we are unable to properly estimate the effects of the various chemical components of infection upon the alterations of the fibrinogen, the fibrin ferment; on the increase in number of leukocytes and platelets, the erythrocytes and their degeneration. Nor do we know whether specific agglutinins (platelets) are produced. Indeed, experimental methods have shown that certain toxins and bacteria have a specific action upon certain parts of the total blood. If we accept the theory that the essential moment in thrombosis is the coagulation, the absence of thrombi in many cases of hemolytic streptococcus infection and the frequent development of thrombi in pneumonia or staphylococcus infection could be explained on a specific toxin effect. Such assumption, however, cannot be admitted as yet, since thrombosis is not merely a process of coagulation.

Even the possibility of a diffuse chemical influence of infectious poisons upon the vessel walls has been considered, and paralysis of the inhibitory activities of the endothelial cells in so far as these have a defensive mechanism against thrombosis. These, however, are speculative theories.

Although infection can thus play a rôle, it is not necessarily followed by thrombosis, unless some other special factor is brought into operation.

Mendel¹ suggested the appellation "thrombophilia" to designate a general predisposition on the part of a patient with infectious disease to thrombosis. This was extended to include that state of heightened susceptibility to thrombosis that may occur after an infection has been overcome. Such an acquired state would be opposed to hemophilia in which an absence of thrombokinase has been believed to occur. There is still some doubt as to the correctness of this assumption.

Various causes² have been given for the tendency to thrombosis in infection. Very few cases of thrombosis occur in the cadaver in which we are not able to demonstrate an infectious malady of some sort as a possible cause. (1) Thrombi are particularly frequent in the neighborhood of infectious processes; (2) in varices, the blood is apt to remain fluid as long as infection in the neighborhood is absent; and whenever a wound in the skin permits

¹ Mendel, München. med. Wchnschr., 1909, LVI, 42.

² Lubarsch, Berl. klin. Wchnschr., March 11, 1918.

of the entrance of bacteria, thrombosis occurs; (3) in post-operative thrombosis, there is usually associated elevation of temperature; (4) microscopic search and bacteriological cultures of thrombi have demonstrated the presence of bacteria; and (5) it has been found possible to produce thrombi in animals by the injection of bacteria.

Kretz states that of 6511 cases he was unable to find a single instance in which thrombus formation was not associated with previous infection. Lubarsch, on the other hand, in his material notes 13 per cent of thrombi in which no infectious process could be discovered. If the remaining number (87 per cent) is critically reviewed for a possible regional relationship between the infectious process and the thrombosis, it appears that only 55 per cent showed any association, and these would have to be still further reduced to 52 per cent if thrombi are excluded that might have antedated the infectious process.

Autopsy material then would suggest that the infectious process plays a considerable rôle in about half of the cases.

How can the action of bacteria be brought into harmony with the usually accepted theories as to the genesis of thrombosis? Firstly, the influence of the infectious agent upon the heart and the circulatory centers; secondly, on the blood and the blood forming organs, particularly the bone marrow; and thirdly, the action on the blood vessel wall:—these are the theories that have been advanced.

If we emphasize the rôle of alterations in the blood constituents as a determinant in thrombosis, the action of organisms in a chemical and morphological sense can be easily brought into consonance with existing theories of thrombus formation. Thus, bacteria not only destroy the red blood cells, but also through their action on the bone marrow, particularly on the giant cells (megakaryocytes) may play an important part. Both red blood cells and giant cells are influential in the formation of blood platelets, be they considered as products or degeneration products. For, it is known that giant cells are thrown out into the blood stream by reason of irritation by bacteria, so that the influence of streptococci, for example, can easily be understood both on the basis of their destroying influence on the red blood cells, as well as on the basis of their irritative effects on the bone marrow.

CHAPTER XXII

GANGRENE—GENERAL CONSIDERATIONS

Gangrene (Fr., *gangrène*, Latin *gangraena*, from Greek *γάγγραινα* an eating sore *γρᾶω*, *γρᾶειν* to gnaw) signifies the death of macroscopically visible portions of the body, the invisible liquefaction of tissue being known as *molecular death* or *ulceration*.

Mortification is synonymous with gangrene, being more frequently used in the parlance of the laity.

Mummification refers to that type of gangrene in which drying or desiccation of the tissues takes place.

Sphacelation means total death of all of an affected part, the dead tissue being known as a sphacelus.

Sloughs are dead masses of tissues, the result of a process of sloughing. The act of sloughing which results in the formation of sloughs may be brought on by ulceration or inflammation. Thus, a core is an inflammatory slough; when it is sufficiently large and possibly putrid, it is termed gangrenous slough.

Properly speaking, *necrosis* is a general term that should include all types of tissue death. Although used in this way by the Germans, in English medical parlance, it is more frequently applied either to the disintegration or death of internal organs, when the mortification is unattended by decomposition, or to the death of bone tissue.

Gangrene is usually the result of impaired or absent blood supply. Other causes, however, must be able to bring about mortification in the presence of a

patent and apparently intact or adequate circulatory system, as in the so-called vasomotor varieties of gangrene, of which Raynaud's disease is an example. It is by virtue of the development of an adequate collateral circulation, that gangrene can be prevented, so that we can distinguish between the clinical picture of impaired or arrested circulation with gangrene as a sequence, and where gangrene has been averted through the development of sufficient secondary circulatory paths.

In addition to the factors, impairment of circulation and establishment of collaterals, other influences may determine the development of gangrene. These are the general condition of the patient and the local condition. An enfeebled general condition, a weak heart, the debilitating effects of prolonged illness, of infection or diabetes, all these, not only lower the vitality, but also militate against recovery. Local conditions such as extravasations of blood, inflammatory exudates, localized vascular disease, stasis or congestion resulting from tight bandages, and improper posture, are additional impediments to the formation of collateral paths. The tissues, too, vary as to their vulnerability, the vitality of bone, cartilage, tendons and fascia being apparently greater than that of muscles and nerves, whilst the glandular organs and the elements of the simple nervous system seem to succumb within a very few hours after complete blockage of the main avenue of blood supply. In certain tissues, such as muscles and nerves, impairment of circulation produces temporary ischemia, which, if not of too long duration, leads to degeneration, functional disturbances, so-called ischemic contracture and palsy, but not to gangrene.

For a thorough comprehension of the clinical manifestations of gangrene or impending gangrene, it is essential to be able to recognize not only the signs that appear when the condition is definitely and well developed, but all those objective evidences of impaired circulation that may precede by months or even years the advent of true gangrene or even of trophic disorder. The signs and symptoms of gangrene and those of impaired circulation will be merely mentioned here, a detailed description being given under the discussion of the various types of gangrene.

Signs of death of a limited part are the following: first, loss of pulsation in the usually palpable vessels; second, coldness of the part; third, absence of sensation or paresthesiae followed later by anesthesia; fourth, loss of active motion in the part, or loss of function; fifth, change in outward appearance, chiefly in color. At first there may be intense blanching, the skin having a waxy, cadaveric or ivory tint. Or, if the part be engorged with blood by virtue of intense venous stasis, a cyanotic livid hue will predominate. Later, the color and appearance of the part will change, as the condition of *dry* or *moist* or *mixed* gangrene is developed.

Premonitory Symptoms of Gangrene.—These are best illustrated when the extremities are the seat of impaired or arrested circulation. *It is quite as important to be cognizant of the objective and subjective phenomena antedating the advent of gangrene or trophic disorder, as it is to recognize the death of tissue itself, for, in most cases in the clinic, the diagnosis of the arterial lesion leading to gangrene should precede by a longer or shorter period the onset of the gangrene itself.*

Symptoms of Impaired Circulation.—Certain definite clinical manifestations of diminished blood supply are frequently the precursors of gangrene. Or, gangrene may occur in one limb and never develop in the other, although both limbs offer the signs of diminished blood supply. The most important of such clinical signs are the following:—

1. *Intermittent Claudication*.—By this term is meant cramp-like pains in the calf of the leg brought on by walking or running, and causing the patient to rest the limbs. The pain regularly disappears when the muscles are in a state of repose. Less typical pain referred to the ball of the foot or the ankle, or the instep, must be regarded as of the same nature. Erb's syndrome called "intermittent claudication" should not be regarded as a clinical entity, for the symptoms described as intermittent limping do not belong to any one group of cases, but occur in almost all of the cases in which obstructive or obliterative disease of the arteries of the lower extremities is present. Thus, intermittent claudication is a symptom of thrombo-angiitis obliterans, athero- or arteriosclerotic disease, arteriosclerosis with diabetes or with thrombosis, or endarteritis, and aneurysm of the popliteal artery. The feeling of *weakness* in the affected part also influenced by motion, properly belongs here, since it is so frequently associated with the pain and cramp-like phenomena. Clinically similar manifestations may have been described (Dejerine) with apparently patent peripheral arteries where a lesion in the spinal cord is held responsible.

2. *Coldness of the extremity*, when chronic, is a significant sign. It may be influenced by climatic conditions and intensified by exertion. It is manifested subjectively and objectively.

3. *Bluish discoloration (cyanosis)* of the tips of one or more toes, particularly the great toe, sometimes of the ball of the foot, intensified by walking and associated with coldness—is another important manifestation.

4. *Ischemia or blanched condition* of the extremity may occur when the limb is in the horizontal position, more rarely in the dependent, but can usually be elicited by elevating the affected limb 60 to 90° above the horizontal.

5. *Redness or rubor* involving the toes, sometimes the dorsal and plantar aspects of the foot for varying distances (to the ankle or even higher), is a feature of diagnostic importance. It frequently involves the lower extremities when these are allowed to hang down, occasionally occurring even in the horizontal position of the limb, and independent of infection, gangrene, or trophic disorder. The author has termed this phenomenon "erythromelia."

6. *Absence of pulsation* usually occurs in the palpable vessels of the extremities, the dorsalis pedis, the posterior tibial, popliteal, or femoral of the lower extremity, the radial, ulnar or brachial arteries of the upper extremity.

7. *Trophic disorders* include indolent fissures, ulcers, hemorrhagic areas, superficial ulcers, perforating ulcers, a withered or atrophic condition of portions of the extremities, foot or hand, and impaired growth of nails.

8. *Thrombosis* may occur in attacks with the following symptoms referable to the sudden closure of vessels; pain in the calf of the leg or foot, inability to walk, pallor of the forepart of the foot, coldness, blanching of the foot on elevation, loss of pulsation in the dorsalis pedis, posterior tibial or popliteal arteries, or all of these, sometimes followed by the development of trophic disturbances, and even gangrene, or at other times eventuating in more or less complete recovery.

CHAPTER XXIII

METHODS OF INVESTIGATION OF GANGRENE

The identification of specific minute architectural peculiarities in thrombo-angiitis obliterans, the understandable and acceptable explanations therefor given elsewhere;¹ the gross and microscopic recognition of the atherosclerotic lesions, the demonstration of constant and immutable differences between the thrombotic obturating changes in the blood vessels, and the hyperplastic endarteritic processes; all these have permitted us to correlate accurately a clinical, pathological and structural classification.

On the other hand, the vasomotor and trophic neuroses, by reason of our imperfect knowledge of anatomic as well as functional derangements of the vegetative and sympathetic nervous systems, must be grouped principally upon a basis of clinical characteristics and similarities.

Since a correct concept of the distinctive clinical features of certain vascular lesions must needs depend upon repeated mental comparative association of the gross and minute visual findings obtainable from the vessels of amputated limbs, with the anamnestic, subjective and the objective physical signs, it is advisable that the student have the opportunity of viewing as many pathological specimens as possible. Through these he should be able to supplement his routine observation with the anatomical complement essential for thorough comprehension. Then, too, will the disassociation of hydrostatic and mechanical factors from the attendant evanescent or transient neurotic symptoms be more readily understood; and then will the striking differences and peculiarities of symptomatology and clinical course in the vasomotor neuroses be better appreciated.

In lieu of actual pathologic material intensive application to the study of the lesions described in other chapters may act as a good substitute.

In consonance with the trend of modern medicine, which is not satisfied with barren labelling and dividing of morbid conditions into classes according to the presence or absence of certain qualities, we must endeavor to supplement clinical phenomena with a well-grounded and searching method of investigation such as will be herein described. It was through the results obtained by it and the hypotheses evoked by its application, that a satisfactory differentiation of the neurotic and the physical symptomatology was made possible.

For the sake of clearness and emphasis let us recapitulate by title what a correct method of approach should include

- (1) The general appearance of the limb
- (2) The presence or absence of rubor or cyanosis in the pendent position of the limb
- (3) The existence of ischemia on elevation of the limb and the interdependence of change of position and blanching
- (4) The absence of some or all of the usual arterial pulsations
- (5) The angle of circulatory sufficiency
- (6) The possibility of eliciting reactionary or induced rubor
- (7) The presence of migrating phlebitis
- (8) The existence of trophic disorders and gangrene, and

¹ The author's interpretation of the acute and chronic lesions in the vessels is given in detail in Chap. LXI-LXII.

9. The other refinements of physical diagnosis or special tests described elsewhere.

Certain salient facts in connection with the distinguishment and classification of the varied clinical morbid complexes here under discussion, deserve mention and careful consideration. Without the correct mental approach in our methods of differentiation, the confusion in diagnosis now so widespread will tend to become perpetuated. Let us then focus our attention on certain essentials that should be borne in mind.

First, there are two distinct, clinically discrete and pathogenetically separable types of morbid process in the extremities, both associated with manifestations of circulatory derangement, exceedingly similar in many of their objective and subjective phenomena. These are the organic and the neuro-pathic affections of the blood vessels or vasomotor, or vasomotor and trophic disorders.

Second, these two forms may be again subdivided into clinical entities some of which represent essentially diverse pathological lesions, others however, corresponding in the present state of our knowledge, to different kinds of derangement in the vegetative and sympathetic nervous systems, the exact nature of which is unknown.

Third, whereas the anatomic alterations in the vessels in the organic type of vascular disease have been satisfactorily classified by virtue of the recognition of gross architectural and histological differences in the blood vessels, and whilst the causal relations between structural changes and symptomatic effects have been explained beyond question, such harmonious relatively has not been established between the characteristic phenomena of the vasomotor affections and the nervous system where the motivating agency is supposed to reside. In the latter, theoretical assumptions alone are offered in the interpretation of the varied and bizarre manifestations, since microscopic and microchemical deviations from the normal have not been obtainable.

Fourth, the *organic* types may be attended with vasomotor phenomena, but the latter do not justify the assumption of the coexistence of the two forms of disease. Some of the appearances imitate true vasomotor symptoms, but are clinically dissimilar under the application of proper tests, and of wholly different origin. Others are veritable vasomotor manifestations, the expression of irritative and exhaustive influences in the sympathetic system, usually of transitory or even fugitive nature, surely of insufficient duration to be recognized as, or segregated into clinical or pathological entities.

Fifth, the *clinical phenomena* attending organic vascular lesions of the extremities when manifested as rubor, ischemia, nutritional and circulatory disturbances—including atrophy, swelling, edema, trophic disorders and gangrene—may not be sufficiently characteristic to permit of precise differentiation from the true vasomotor affections. Even with additional subjective data, decision may not be possible. It is through an investigation of the *circulatory functions* in the affected limb in the manner previously described that pathognomonic signs may be obtained. The dictum to refrain from diagnostic conclusions based on anamnestic and visual information alone, is applicable here, and worthy of the strongest emphasis. Any scheme which has the identification of the various interrelated or even completely diverse morbid entities in view, is inadequate and unsatisfactory unless the data obtainable through physical examination are accorded due weight and consideration.

Before proceeding to the discussion of the various forms of gangrene and to the symptomatology, pathology, diagnosis, and treatment of both organic and neurogenic morbid processes that result in, or threaten to bring about tissue death, it may be well to dwell more in detail on some of those salient phenomena upon which their advent is often foretold. These are *pain*, *arterial pulsation*, and "*intermittent claudication*." The other phenomena already alluded to, namely the coldness of the extremity, cyanosis, lividity, ischemia, rubor or erythromelia, trophic disorders, and thrombosis shall receive more comprehensive attention under each and every separate malady in which they may present themselves.

CHAPTER XXIV

DIAGNOSTIC SYMPTOMS—ARTERIAL PULSATION

The detection of the presence of pulsation in the palpable arteries of the extremities, namely the ulnar, radial, brachial, dorsalis pedis, posterior tibial, popliteal and femoral—is one of the most valuable physical signs for the recognition and differentiation of a symptom-complex due to vascular disease or of vasomotor incitement. Whilst the pulse in the above mentioned arteries of the upper extremity can usually be elicited in the normal individual except aberrant radial and deep seated ulnar vessels, a number of extraneous conditions, seem to influence the demonstrability of the pulses in the lower limbs. Both an anomalous course as well as concealment through adiposity can invalidate the palpatory physical findings.

The incidence of pulsation in the normal has been investigated by Erb's assistants, who found that single pulses eluded detection, in somewhat less than 1 per cent of the 700 ward cases that he examined. In the author's experience, tests of some 200 cases—that were regarded as normal, and in which the possibility of any excessive compromise of arterial integrity could be excluded—failed to evidence more than one instance of absence of the dorsalis pedis pulsation ($\frac{1}{2}$ per cent).

Therefore, the demonstration of palpable evidence of obliteration through the disappearance of pulse, is to be accorded great weight as a sign of organic vascular occlusion, particularly if elicited at a period free from possible vasomotor spastic phenomena and demonstrated repeatedly under varying circumstances.

Fortuitous interference with the demonstrability of the arterial beat through changes in the skin, as edema, eczema, elephantiasis, adiposity, and other exceptional causes, must be given proper consideration.

The popliteal pulse can be best felt in the following manner: With the patient prone and the leg flexed to the vertical and with muscles relaxed, the examining fingers enter the upper half of the popliteal space where the vessel can be readily discovered by pressure downward against the femur (Fig. 42). It is only in very stout individuals that pulsation fails to manifest itself in non-occluded arteries.

Elsewhere will be discussed those occasional examples of vast functional exclusion of the arterial tree, where the femoral, popliteal, posterior tibial and dorsalis pedis pulsations are imperceptible, and in which arterial obliteration of indeterminable nature is believed to exist. Enough clinical observa-

tions are at hand to bear testimony to the view that embolic closure of some of the larger arteries of the extremities may take place with apparently no symptoms, or such minimal ones as to completely escape the notice of the patient. This conclusion has been arrived at through the study of incipient clinical stages of embolic obturation of larger arteries in patients already under observation for definitely proven embolic or thrombotic gangrene of another extremity. With the sudden advent of the signs of impaired circulation in a foot, or with a vague history of pain and coldness of abrupt onset, the

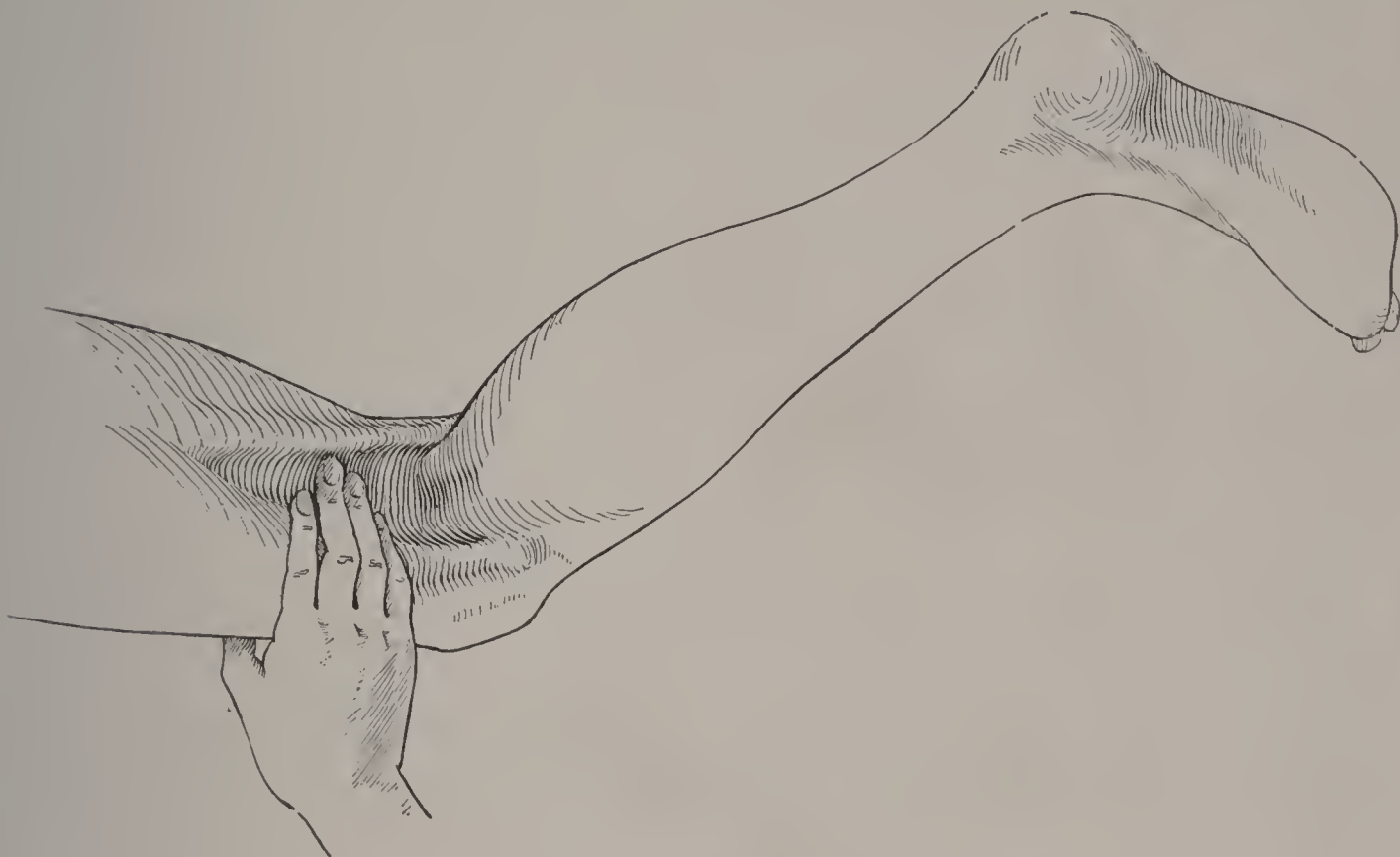


FIG. 42.—Author's method of palpating the popliteal artery.

absence of pulses and other phenomena makes the diagnosis clear. And still, by virtue of the developing collateral channels, all evidences of circulatory disturbance may disappear except the absent pulses; and a clinically unrecognizable phase may then present itself to a future observer. For such, the clinician will have but the altered pulses and the accompanying manifestations, if any, to guide him. The history of trouble in another territory may be an aid; but only a vague record, if any, in the limb now examined will be at his disposal.

Two types have come under our observation.

(1) Embolic closure of a large artery of the lower extremity, symptoms of imminent gangrene, rapid and adequate substitution of the collateral circulation, a latent or functionally cured stage, without trophic lesion being the issue.

(2) Embolic closure of the posterior tibial artery above its bifurcation in cases of multiple emboli of the extremities, with an identical sequence.

A more complete discussion of this subject will be found in Chap. LII.

Whilst the absence of pulsation at the usual palpable sites may be regarded as indicative of arterial closure in most instances, the existence of pulsating vessels does not preclude vascular obturation in certain other territories. Both clinical observation and pathological examination of amputated limbs have conclusively shown that extensive closure of the plantar arteries and even the digital and dorsalis hallucis can exist, whilst the posterior tibial,

dorsalis pedis and anterior tibial arteries pulsate strongly. Clinically too, the usual symptoms of thrombo-angiitis obliterans and even gangrene may be coincident with pulsating vessels, when the plantars alone are affected. As the disease progresses, both the posterior tibial and dorsalis pedis may become occluded.

Many observations, clinical, operative and anatomic through dissections made by the author attest to the fact that arteries in which pulsation is usually perceptible may fail to beat, although at the site of palpation their patency is conserved. Blood may trickle or flow through such channels without pulsative effect on the vessel wall. So in a case of embolism of the brachial artery, in which arteriotomy and embolectomy were performed (Chap. LXXXV) the flow through the section beyond the obstacle could be readily demonstrated. Exceedingly interesting and conclusive evidence was also obtained in another case of embolectomy of the brachial artery, where, although an additional more remote territory was opened, by removal of the clot, the radial pulse remained abolished, not to return until 7 months after the occlusion.

Absence of Pulsation Distal to Occlusive Thrombi.—That the absence of pulsation does not always indicate organic occlusion, but may signify empty vessels distal to the occlusive embolus or thrombus, has been frequently observed in thrombo-angiitis obliterans and may also occur in cases of embolic gangrene of cardiac origin or in thrombosis complicating atherosclerosis. It will be pointed out elsewhere how *the return of circulation through collaterals* demonstrates the patency of such seemingly closed vessels, and how this *reappearance of pulse* has often been misinterpreted as evidence of the beneficial results of treatment.

Here it may be well to emphasize the occurrence of imperceptible pulses beyond the point of thrombotic occlusion in cases of atherosclerosis. As an example may be offered the following interesting case.

J. R., male, aged 47, diabetic with advanced atherosclerosis; sudden advent of gangrene of the right foot and leg with absence of pulsation in the popliteal, femoral and external iliac arteries for a distance of about 1 inch above Poupart's ligament.

Amputation below the level of the origin of the profunda artery through the upper fourth of the thigh. At this level the femoral artery was partly closed by atherosclerosis, partly by recent thrombosis; almost no bleeding at this level, amputation being performed without a tourniquet or Esmarch. Five days after the operation a strong pulse could be felt in the femoral artery down to within about $\frac{1}{2}$ inch from the point of section, the wound having been left wide open.

In explanation of the return of such a pulse, two theories can be advanced; one, that the occlusive thrombus in the external iliac was dislodged into the femoral just above the point of ablation, or that the common and upper superficial femoral had been patent; and that through establishment of the collateral paths the pulse became reestablished. The latter is in the author's opinion the correct explanation, since the character of the thrombi and their age would preclude their having been detached after the amputation. Similar reestablishment of circulation is described elsewhere as occurring in the vessels of the upper extremity after embolic closure of the brachial artery.

CHAPTER XXV

DIAGNOSTIC SYMPTOMS—PAIN

Pain is such a varied phenomenon both as regards its appearance, constancy, methods of excitation in the organic and neurogenic forms of arterial affection of the extremities, that it may be well to analyze its method of origin and some of the characteristics in the maladies in which gangrene may occur.

In *erythromelalgia*, it is interesting to note that in the majority of the cases the pain does not follow the path of any of the peripheral nerves, nor is it encompassed within the territory or distribution of any nerve root. Furthermore, in the quality of the pain there seems to be a difference here as contrasted with the common neuritic and neuralgic forms of pain. There is a deep-seated burning, poorly limited, constant, susceptible to exacerbations that is quite different from the pain described in the neuralgic cases. A similar condition is noted in cases of frozen extremities, when they suddenly enter into a warm room, the blood rapidly returning. This would arouse the suspicion that the pain is related to alterations in the vessels.

Centripetal conducting elements of the sympathetic (Chap. IV) are numerous according to anatomical investigations. It would not be too audacious, therefore to believe that irritation of the centripetal fibers may evoke pain. If we accept the notion of the possibility of pain of sympathetic origin, we must seek a special form of irritant for the excitation of such pain. This is true, since in affections of the sympathetic nerve of the neck, excitation leads to mydriasis, and narrowing of the vessels without pain.

We may assume that in certain *arterial diseases*, such as arteriosclerosis, irritation of the sympathetic plexus in the adventitia could cause stimuli that are transmitted or transferred in the spinal segments to sensory tracts, causing the so-called referred pain. But we cannot exclude the possibility that pain may be occasioned by alteration of the centripetal nerve fibers emanating from the blood vessels themselves, even though these under ordinary circumstances do not carry such impulses.

In *erythromelalgia* it is possible that pain is occasioned by direct irritation of the sensory sympathetic elements in the vessel wall; for, the vasomotor and sensory symptoms often occur almost simultaneously in this condition.

In *thrombo-angiitis obliterans*, the acute pain that is associated with the attacks described as the attacks of acute thrombo-angiitis obliterans, may also be, and probably is of the same origin. The vessels themselves become painful. This pain is of a different nature from that which is associated with exercise (intermittent claudication) and that which precedes and attends the development of trophic lesions of the distal parts. Impulses along the usual sensory paths would account for the pain accompanying ulcers, fissures, and gangrene; but even here the abnormal intensity of the sensory impressions would lead one to believe that a distinct alteration in the threshold for pain often exists.

In *Raynaud's disease* sensory phenomena, be they anesthesia, hyperaesthesia or pain, do not correspond to the territory of a single nerve, but extend rather diffusely over the extremity, being rather confined to the area in which there are vasomotor and trophic disturbances. The difference noted is that the pain is apt to extend farther proximally, and radiates to a greater degree

towards the root of the extremity. The absence of relation between its situation and the course of distinct nerves, the diffuse distribution, the simultaneous occurrence of pain in both extremities, and its extension into the deeper tissue, these are facts that speak for a more central lesion. Because of the return to normal in certain cases, and the transitory nature of the symptoms, Cassirer concludes that in the Raynaud complex there may be lesions that are easily repaired, possibly superinduced by vasomotor influences and their consequent trophic effects. This assumption, however, could only be extended over a limited number of cases.

In most of the cases of true Raynaud's disease an exact localization of the lesions cannot be made. The nature of the pain and its distinct relationship to vasomotor phenomena point to a very evident association with the vasosensory fibers.

In *organic obstructive arterial diseases* various explanations may be given for the relationship between the advent of pain and its intensity to the position of the limb. It is usual (though not without exception) to find that pain will be evoked whenever the limb is elevated sufficiently long to produce a very marked ischemia, or at least, if this position be maintained over a sufficient period of time. It is impossible to assert just how important is the ischemia itself, with its power to cause irritation of the sensory nerves, and to what extent the secondary reflex or direct spasm of the vessels is an exciting moment. Doubtless both agencies may play a rôle.

Paroxysmal pain of a diffuse variety is occasionally severe; it may come on in insufferable nocturnal attacks, especially in those arteriosclerotic cases in which recent thrombosis has been superadded. No satisfactory explanation for this manifestation has as yet been presented. Possibly it results from a summation of the excitant action of cumulative chemical effects, or of prolonged circulatory stasis. The latter would be favored by inactivity during resting (sleeping) periods, and might attain a climax sufficient to incite spasm in still non-sclerotic smaller arteries (discussed more fully in Chap. XXVI).

This phenomenon would be analogous to that of intermittent claudication, but of different causation—a paradoxical intermittent claudication of *inactivity*.

The pain induced by prolonged pendency of the limb, particularly if this position be preceded by a period of elevation, is perhaps more difficult to account for. It is not uncommon to find patients who are unable to allow the legs to hang down for a protracted period, particularly if well marked rubor and trophic ulcers or fissures be associated phenomena. Here, we may presuppose inadequate oxygenation of the blood as evidenced by the ensuing lividity when the posture is continued. The manifestations do not seem to be unlike those that are expressed by tingling, formication and pain in the fingers of a person who had exposed them to excessive cold; or in whom a constricting (Esmarch) bandage had been applied and released. In such a case the effects of ischemia and subsequent hyperemia or even stasis, cause responses in the sensory nerves. Or, perhaps, even the vascular channels, themselves are the source of sympathetic sensory impulses. In the present state of our knowledge we must be content to attribute to both the inherent vascular nervous paths and also to the sensory nerves a rôle in the incitement of the above types of pain sensation.¹

The alteration of tonus (change in threshold) in the spinal cord that may be produced by persistent pain and its influence on vasomotor stability are

¹ A more detailed statistical and clinical description may be found under the Chapters on Thrombo-angiitis obliterans.

discussed elsewhere.¹ It is not infrequently stated that the distress is especially intense at night. This may be in part due to variation to threshold for pain perception; but it is in part referable to the lack of motion and resulting stasis.

The pain associated with *trophic disorders*, such as ulcers over the distal parts of the phalanges, may be exceedingly intense and quite out of proportion to that which we would expect from lesions of similar nature and extent complicating other affections. It is apt to be noteworthy in its degree in thrombo-angiitis obliterans, and may be so excruciating as to render the patient neurotic and to beg for amputation of a toe or even of the leg. The threshold for the pain sense is indubitably altered in these cases, and a condition of hyperexcitability of the sensory domain probably exists. Indeed, persistence of pain of similar nature may continue for days or weeks after amputation of the limb.² On the other hand, it is reported that injection of absolute alcohol into the posterior tibial nerve may completely abolish pain attending trophic ulcers of the foot. Whilst no doubt is cast on the correctness of such observations, it is difficult to reconcile this therapeutic effect with the above statement of the persistence of pain after amputation.

CHAPTER XXVI

DIAGNOSTIC SYMPTOMS—INTERMITTENT CLAUDICATION

Thoroughly intrenched in medical parlance, this term, though giving rise to much confusion, may still be retained, if its import, limitations, and exact significance be comprehended. Suggested by Erb as applicable to a distinctive clinical picture, it has by virtue of incorrect interpretation, been transferred to a multitude of affections, the true nature of which has oft been unrecognized, and has been confounded with Raynaud's disease. Although believed by some to denote morbid entity, it should more properly be confined and restricted, as a designation for a *complex of symptoms*, such as may be associated with a number of different pathological processes, or even vasomotor affections. In this sense, not indicative of any particular disease, but as a composite of manifestations, it will be used by the author. That there may be an association of other manifestations of vasomotor neuroses or that it may itself be of neurogenic origin cannot be denied. Nevertheless, much progress will be made in the differentiation of vascular affections of organic from those of neurogenic derivation, if the limitations above suggested be adhered to.

SYMPTOMS

The characteristics of the Erb type of intermittent claudication are complete or almost complete absence of pain or discomfort in a limb when at rest, commencement of disturbances, pain, tension, paresthesiæ, weakness shortly after walking is begun, gradual intensification of these until walking is embarrassed and finally impossible, and the disappearance of the disorders

¹ See page 42.

² See page 259.

after a period of rest. Objectively there may be coldness, cyanosis, transitory patches of rubor interspersed with the cyanosis, with a marmorated appearance of the skin. At times cadaveric ischemia is noted: one or more arteries of the foot usually fail to pulsate. Trophic disorders such as dry skin, ungual dystrophies and gangrene may complicate the picture.

This is the *symptom-complex* as it is associated with *organic vascular disease* in contradistinction to the angiospastic or *functional variety* that is to be grouped with the *vasomotor neuroses*. This description of a symptom-complex is incorrectly extended to include a number of diverse infections.

Intermittent claudication may be described as a *manifestation* accompanying two totally diverse processes:

- (1) Vasomotor neuroses (angiospastic neurosis); and
- (2) Obstructive arterial disease (arteriosclerosis, thrombo-angiitis obliterans, etc.)

Oppenheim¹ distinguishes a (1) benign and (2) malignant form, the former a functional or purely angiospastic phenomenon, the latter associated with diseased arteries.

I. *The Vasomotor Type*.—A concomitant neurosis of the neuropathic diathesis, is said to coexist with *intact* arteries and to depend on spasm of the arterial wall. Oppenheim mentions the following characteristic instance in which transitory pain on walking with disappearance of pulse, coldness and blueness of the toes were significant.

A male thirty years of age had been suffering for two years from painful sensations in the feet on walking, these becoming gradually more severe so that at time cramps and numbness in the feet and legs were pronounced even after fifty paces. After walking two hundred steps in the office, painful fatigue with coldness of the skin and bluish discoloration set in, together with a disappearance of both dorsalis pedis pulses (?). After a rest of a minute, the right dorsalis pedis pulse was again perceptible. Several years later, all the symptoms had disappeared, and the *arteries of the foot were distinctly discernible*.

Another case quoted by the same author is equally valuable.

Miss S., 22 years of age had frequent attacks of local syncope in her finger since her sixteenth birthday. In the winter of 1898 there was much emotional strain, and in the early summer of the same year she took a long and arduous tramp. Immediately after this, the following condition developed. After walking 100 to 200 steps she experienced severe pain and coldness in the left leg, and to a lesser degree in the right; the calf of the leg seemed to become stiff and there were pricking and stinging sensations. After standing still for a few minutes, she could go on again for a short time. The patient was a slender, anemic individual. The *pedal pulses were present* though weak. When the patient was allowed to walk around the room some 15 to 20 times, *the foot became pale and bluish, and the dorsalis pedis pulse was no longer perceptible*. Five to 10 minutes later the beat returned.

These forms may have to be differentiated at times from Raynaud's syndrome and erythromelalgia. When the angiospastic phenomena affect not only the territory of the muscles but implicate the cutaneous arteries, vasomotor manifestations in the integument appear that may mimic the above conditions.

The points valuable in differentiation are: In *intermittent claudication*, the dependence on motion is characteristic even though the picture is obscured by evidences of vasomotor irritation (blanching, cyanosis and reactive rubor), and the temporary or permanent absence (?) of pulses; in Raynaud's, the spontaneous, symmetrical and paroxysmal appearance with patent arteries is the rule.

Whilst the careful observations of eminent authorities on the occurrence of the *angiospastic*, *functional* or *vasomotor* type of intermittent claudication deserved respectful consideration, a study of a large number of cases of

¹ Oppenheim, Deutsch. Ztschr. f. Nerven., XLI, p. 376.

organic disease of the vessels of the lower extremity, has convinced the author that the *incipient stages of true vascular obliteration when accompanied by similar symptoms is frequently overlooked, and interpreted as a vasomotor affection.*

II. *The type accompanying organic vascular disease* is seen in athero-, arteriosclerotic and syphilitic affections as well as in thrombo-angiitis obliterans. Here the attendant vasomotor phenomena must not be regarded—as Erb would have it—as integral elements of the syndrome, intermittent claudication, but as irritative manifestations, frequently due to external thermal influences, emotions or other excitants. *The associated vasomotor symptoms should not be regarded as part of the Erb complex, since they are present even when the symptoms of intermittent claudication are wholly absent.* The grouping of vasomotor signs with the spasmodic and sensory phenomena of Erb, is insufficiently warranted, therefore, and it is for this reason that the author shall merely include the sensory symptoms in the designation “intermittent claudication.” Cases of organic vascular disease, such as thrombo-angiitis obliterans, therefore, may present vasomotor phenomena, side by side with these regarded as “intermittent claudication.”

HISTORICAL

Keeping in mind that many authors have described intermittent claudication as a morbid syndrome of varied pathogenesis,¹ it may be well and of historical interest to recount some of their observations.

In 1858 Charcot described a clinical picture typical of intermittent claudication. A male 54 years of age complained of weakness, numbness, cramps and stiffness in his right leg after walking for about one quarter of an hour. After a pause of some 5 to 10 minutes, walking would again call forth the symptoms.

The relationship between these manifestations and similar occurrences in animals previously described by veterinarians, was noted and commented upon by Charcot at that time.

Erb gave a classical and extremely illuminating description of the symptoms in the year 1892. A number of different designations and appellations had been employed by various authors, amongst which may be mentioned the following:

Charcot² described a *Claudication intermittente par oblitération artérielle*; and also, *Paralysie douloureuse ischémique*. Erb³ suggested *Dysbasia intermittens arteriosclerotica*; Higier,⁴ *Angiosklerotische paroxysmale Myasthenie*; Oppenheim,⁵ *Dysbasia angiosclerotica*; Walton⁶ and Paul, *Angina cruris*. Grossman,⁷ *Angiosklerotische intermittierende Muskel Parese*; and Determann,⁸ *Akinesia or Dyskinesia intermittens angiosclerotica*.

Charcot had previously called attention to an affection in horses that had its analogy in the human, and to which he assigned the term “Intermittent Claudication.” Boullay⁹ had noted—as had also other authors, subsequently (Rademacher,¹⁰ Böther,¹¹ Vötsch,¹² Sommer¹³ and Goubaux¹⁴) that an ischemic condition of the hind legs regularly appeared as a causal or concomitant phenomenon, so that it was *a priori* clinically acceptable to surmise that impaired circulation could also account for similar symptoms involving the muscles of locomotion in the human.

¹ Erb, Deutsch. Ztschr. f. Nervenhe., 13, 1898, 76.

² Charcot, Compt. rend. Soc. de Biol., 2, Série 12, 1858, p. 225.

³ Loc. cit.

⁴ Higier, Deutsch. Ztschr. f. Nervenhe., 19, 1901, S. 438; Neurol. Zentralbl., 1910, 911.

⁵ Oppenheim, Deutsch. Ztschr. f. Nervenhe., 17, 1900, S. 317; Deutsch. Ztschr. f. Nervenhe. 41, S. 376.

⁶ Walton, Boston Med. and Surg. Jour., 146, 1902, p. 351.

⁷ Grossman, Deutsch. Arch. f. klin. Med., 66, S. 500.

⁸ Determann, Deutsch. Ztschr. f. Nervenhe., 24, 1905, p. 152.

⁹ Boullay, Ac. roy. de Méd. Séance du 11 Oct., 1831. Arch. gen. de Méd., 1831, XXVII, p. 425.

¹⁰ Rademacher, Gwilt u. Hertwig's Magazin f. d. ges. Tierheilk., 1838, IV, S. 455.

¹¹ Böther, Ztschr. f. d. ges. Tierheilk., 1839, VI, S. 425.

¹² Vötsch, Herings Repertorium d. Tierheilk., 1839, VI, S. 425.

¹³ Sommer, Gwilt u. Hertwig's Magaz. f. d. ges. Tierheilk., 1843, IX, S. 461.

¹⁴ Goubaux, Recueil de Méd. Vét. prat., 1846, XXIII, p. 578.

In the so-called "Boiterie intermittente des chevaux", (intermittent limping of horses) one may observe that an affected horse presenting no symptoms at rest or when going at a slow pace, will, after five to fifteen minutes of hastened gait or trot, drag one or the other hind leg. Even a short run may cause it to perspire, and to turn its head in the direction of the hind quarters. Its expression becomes anxious and breathing is accelerated. In short, all the signs of pain, and weakness in the limping extremity become evident. The affected limb becomes simultaneously cold and pulseless. If the horse be now driven still further, the functional enfeeblement may increase to such an extent, that the horse breaks down completely, lying helpless and paralyzed. After a pause or rest of five to thirty minutes it becomes wholly restored and capable of assuming normal pace. Since such attacks recur whenever the animal moves at a moderately rapid gait, the horse becomes practically useless.

Autopsies have revealed an obliteration of the distal portion of the aorta in the bilateral cases, and closure of the iliac or femoral artery in unilateral, when one limb alone is involved. Gangrene does not occur because of the relatively favorable conditions that obtain for the establishment of a collateral circulation.

In Charcot's first and analogous case an aneurysm of the right iliac artery with obliteration of the distal portion of the artery was present. This aneurysm and consecutive thrombosis had followed a bullet injury sustained some twenty-one years previously.

Curiously enough this first reported and clinically observed case of intermittent claudication in a human being had for its anatomical basis a most uncommon lesion, since, as subsequent investigation revealed, symptoms of intermittent claudication usually accompany and are due to disease of the *peripheral* vessels of an extremity (Erb).

CLINICAL TYPES

Although the organic vascular form of intermittent claudication seems to be the most common, the literature abounds in clinical examples warranting the recognition of additional types. We may summarize.

- I. Charcot—Erb's variety (Dysbasia angiosclerotica intermittens).
- II. The functional vasomotor type (Oppenheim).
- III. Intermittent claudication in other territories.
- IV. Acute forms (so-called) probably thrombo-angiitis obliterans, or
- V. Apokamnosis or artificially induced intermittent claudication.

I. DYSBASIA ANGIOSCLEROTICA INTERMITTENS

This type (according to the literature), includes the typical symptoms associated with diseased arteries and has been variously called, claudication intermittente par obliteration artérielle (Charcot). Paralysis douloureuse ischémique (Charcot), angiosklerotische paroxysmale Myasthenia (Higier), angiosklerotische intermittierende Muskelparese (Grossmann), and Angina cruris (Walton).

Whilst the symptom-complexes here described are alluded to by most authorities as indicative of a morbid condition of which they are the most important manifestations, the author wishes to emphasize in advance that he cannot subscribe to such a view. For he will show that intermittent claudication is more correctly merely a designation for *a group of associated phenomena* that may be evoked by a number of varied and diverse pathological conditions. Nevertheless, for a thorough comprehension of the subject it may be well to give a brief review of the symptomatology, etiological factors, clinical course and pathology, as they have been set forth by other authors.

Oppenheim and Cassirer¹ describe the following picture. The manifestations begin slowly as a rule, affecting both lower extremities simultaneously, or successively one and then the other after varying intervals in different

¹ Cassirer, *Loc. cit.*

cases. First, there appear sensory symptoms such as disagreeable sensations in the foot, toes, soles, and calf of the leg with paresthesia, or with a feeling of coldness, alternating possibly with burning sensations, sensory symptoms in the foot or calf of the leg—all of these, or a combination of several developing after walking, and disappearing after repose. Vasomotor symptoms are frequently associated at the very onset of the symptoms, the patient noticing that the feet become blue and cold, sometimes strikingly cyanotic after walking, or when allowed to remain in the pendent position for some time. Such discoloration may alternate or be associated with areas of redness, or the toes may become ischemic. These vasomotor phenomena also are apt to be intensified or appear only after locomotion.

Cassirer remarks that as the pain and cramp-like sensations increase, the muscular disturbances become intensified, so that the patient can walk only with difficulty. In this stage frequent rests become necessary, and finally walking may have to be given up altogether until the symptoms have wholly abated. Such recovery after rest comes on after several minutes, when a continuance of locomotion is resumed with the greatest difficulty. There may be considerable variations in the degree of suffering and functional interference.

Subjective manifestations of vasomotor nature were noted in 25 out of 36 cases. As a rule there was a feeling of coldness whilst more rarely the opposite condition obtained. Local ischemia particularly over the plantar aspect of the feet could be evoked by permitting the patient to walk rapidly around the room, when sensory and motor derangements could also be elicited.

Goldflam¹ states that some of the latent cases of intermittent claudication can be recognized by noting the onset of vasomotor symptoms after exercising the feet and legs. Thus he describes changes in the color of the feet, blanching, disappearance of the small veins with collapse of the veins. In the advanced cases the feet and lower legs may present a spotted cyanotic appearance with possibly hyperemic areas between the patches of cyanosis, the skin temperature usually subnormal, rarely elevated.

Erb, Cassirer and others speak of the absence of the dorsalis pedis and posterior tibial pulses as the most important objective signs. In most of the bilateral cases all four pulses of the feet are wont to be missing.

In the clinical picture above described, it is remarked by a number of authors, that symptoms other than those mentioned are generally absent. The reflexes are usually normal, objective sensory disturbances do not occur and there are no neurologic findings. However, certain trophic disturbances of the skin of the feet may be noticeable, such as dystrophy of the nails and ulcers. Very frequently a decided degree of arteriosclerosis can be detected.

Two facts stand out prominently as having a causal relationship with the symptom-complex: first, certain circulatory and vasomotor phenomena; and second, the absence of the pedal and crural pulses.

The circulatory and vasomotor phenomena that usually precede the manifestations of intermittent claudication and may be given the importance of prodromal signs, are described as attacks of peculiar paresthesiæ (feelings of heat and cold, formication and sensation of "falling asleep") with cyanotic, livid, marmorated or cadaveric discoloration of the foot and leg. The same interdependence of symptoms and locomotion, as noted with intermittent claudication obtains in the production of these visible signs. When the well marked motor disturbances of intermittent claudication are

¹ Goldflam, Neurol. Centralbl., 1910, S. 1.

fully developed, such objective and subjective paroxysms as here given may appear simultaneously.

Coldness, cyanosis and pallor of the affected parts are noticeable when the patient complains of numbness or strange feelings in the toes.

Erb called attention to the fact that in the well developed cases the feet are apt to show abnormalities in appearance, even with the absence of paroxysms, that is, during the free intervals. When the extremities are allowed to hang down, they are apt to be cold, cyanotic, swollen. The skin is said to be abnormally dry, and the growth of the nails impaired. Bright red spots may be interspersed with the cyanotic areas, lending a marble-like appearance to the skin. Or, anemic areas may appear usually involving one or more toes, the feet becoming cadaveric and cold for varying periods of time, these phenomena being associated with prickling or sticking sensation when the normal redness or cyanosis returns. All these manifestations may be absent when the patient is at rest in bed, or in a warm temperature. *All of these appearances, we believe, may belong to any of the types of organic arterial disease, and cannot, therefore be regarded as a separate entity.*

Examination of the Pedal and Crural Arteries.—This may be regarded as of pathognomonic value in the diagnosis of dysbasia, angiosclerotic intermittens. The absence of pulses in one or more of the four pedal arteries is almost a regular finding, and may be accompanied by demonstrable thickening and tortuosity of the vessel. Thus Erb reports that of 30 bilateral cases there was an absence of the beat in all four arteries in 16 cases; three in 2 cases and in 1 case absence of one pulse. All four pulses were palpable in but 4 cases, and in these they were weak, three of the patients having evidenced thickening and sinuous vessels. Of 16 unilateral cases absent pedal arteries were noted in 13.

Almost as important according to the above author is the examination of the popliteal and femoral arteries which often give positive findings, such as absent beat, or the above-mentioned organic changes. In the case of Bourgeois¹ there was an aneurysm of the popliteal artery. Simon² recorded similar symptoms in a case of embolus of the anterior tibial artery. Although a number of observations definitely offer conclusive proof that localized arterial disease such as aneurysm, embolism, etc. can also cause the symptoms of intermittent claudication, as a rule a more diffuse impairment of the circulation as produced by obstructive diseases of the peripheral arteries of the lower extremities is present.

Clinical Course.—A perusal of the literature convinces one of the fact that a progressive and obliterating arterial infection is usually present. Striking also is the circumstance that spontaneous gangrene of the affected extremity is so frequently the issue. In the cases that are not treated, or in those which were refractory to all measures, there was described a progressive aggravation of the condition, or periodic recurrences with increasing intensity of symptoms, finally eventuating in almost complete abolition of locomotion. With increasing intensity of the degree of circulatory disturbance and the concomitant symptoms, gangrene of the toes of the foot, with proximal extension, is said to occur.

II. FUNCTIONAL VASOMOTOR TYPE (OPPENHEIM)

Nothnagel³ recorded the following symptom-complex in a patient in whom the arterial circulation of one arm was impaired by reason of thrombosis of one of the axillary arteries.

¹ Bourgeois, F., Thèse de Paris, 1897.

² Simon, Deutsch. med. Wchnschr., 1905, **19**, p. 754.

³ Nothnagel, Berl. klin. Wchnschr., 1867, No. 51, p. 536.

A girl of twenty-five years was afflicted with striking fatigue, weakness, with pain and paresthesiæ in the fingers and hand on doing but the lightest of work, all symptoms disappearing after a rest.

Such observations confirm the assumption that any occlusive process in the arteries may serve as the basis for the manifestations of intermittent claudication. Therefore, not only the extremities, but other territories should offer clinical evidences of corresponding symptoms.

Doubtless many of the cases of so-called vasomotor or angiospastic forms of intermittent claudication belong more properly to the *vasomotor neuroses*, intermittent claudication being only one of the manifestations, just as are cyanosis, ischemia and other phenomena. That Oppenheim¹ had been compelled to take this view and to renounce, in part, the classification of intermittent claudication previously suggested, was due to the publication of cases that were quite different from the classical forms of intermittent claudication, except for some of the motor and sensory symptoms.

Thus, Westphal² called attention to spastic phenomena in the vessels of the lower extremity with disappearance of the anterior tibial and posterior tibial pulses during the attacks, (coincident with disturbances in locomotion)—in a case of hysterical pseudotetanus—a complex which surely cannot be classed with intermittent claudication, but which, because of the wide and indiscriminate application of this term, had been considered as another variety.

In a woman with symptoms of pseudotetanus, there were associated attacks of vasomotor manifestations involving the upper as well as lower extremities. At the beginning of a paroxysm, there was a pricking sensation in the fingers or the toes, gradually increasing in intensity to actual pain. At times the whole of the hands and feet would be involved, or but parts of these, either on one side or symmetrically. The affected regions would become cyanotic, or violaceous in color, or sometimes ischemic, pale and cold. Pallor would occasionally give way to cyanosis, and a deep prick with a needle could not entice a drop of blood to the surface. Variations in color would be manifold in distribution of time of appearance and duration.

Most striking was the *disappearance* of the pedal beats during such attacks, whilst during the free intervals the feet were found normal, both as to color and as to the intensity of the arterial pulsations. The radial pulses, however, were always present.

With the advent of these vasomotor phenomena, disturbances in locomotion were also noted. The patient would complain some time before the beginning of an attack of *fatigue on walking* and paresthesiæ in the feet. With the actual onset of the attack, walking would become impossible.

What an exquisite example of a pure vasomotor neurosis and how futile to force a clinical relationship between this disease and "intermittent claudication!" That some of the cases described as intermittent claudication were said to have had evidences of an angiospasm in the pedal arteries, cannot be denied; but that the case of Westphal has any clinical or pathological affiliation with either the so-called organic or the functional types of intermittent claudication, is to be doubted.

Record of an instance that was said to be due to toxic factors is that of a young man, in whom the symptoms of intermittent claudication seemed to depend upon psychic or emotional states (Schlesinger³). The symptoms disappeared after one and a half years, only to return eight years later.

Perhaps the most convincing example of the neurotic type of intermittent claudication is a case in which symptoms of this disease were associated with

¹ Oppenheim, Deutsch. Ztschr. f. Nervenhe., 1900, Bd. XVII.

² Westphal, Berl. klin. Wchnschr., Dec. 9, 1907, XLIV, p. 1567.

³ Schlesinger, Deutsch. Ztschr. f. Nervenhe., Bd. 41, p. 235.

the Raynaud phenomenon. The following description and case report will elucidate.

Angioneurotic Intermittent Claudication with Raynaud's Disease of the Fingers.—An example of so-called neurotic intermittent claudication is described (Rülf¹), in which there were combined Raynaud's disease of the fingers, intermittent claudication of the lower extremities, rubor of the tip of the nose and symptoms of migraine.

A woman 30 years of age, always of nervous temperament, began 6 years previously with severe attacks of migraine.

For the past 2 years the tips of the fingers would become numb and white as if dead. Rubbing or motion would restore the circulation. At first the fourth and fifth fingers were involved, later the others. For about 3 months the attacks of syncope were followed by asphyxia. The severity of the symptoms has been increasing; recently have been appearing several times weekly.

The symptoms referable to the lower extremities antedated those of the upper slightly. There have been associated cardiac symptoms, in that attacks of weakness, feeling of faintness and prostration come on after walking. Recently pain has developed in the left leg after walking, necessitating frequent periods of rest. After a short walk, a feeling of tiredness appears in the left sacral region, the weakness and tiredness advancing so as to implicate the left thigh, knee and upper part of the leg. If the body were supported by the right limb, the left leg seemed *warm* again, and the symptoms would disappear.

The dorsalis pedis and posterior tibial arteries could be found pulsating, but were "difficult to find" (?). The radials arteries were abnormally small.

The temperature was found reduced over the left leg and foot, but not always, usually only after walking. The blood pressure was 115 systolic.

This case is described as one of intermittent spasm of the *vascular capillaries*, since the pedal pulses were neither diminished nor abolished during the attacks. The diminution of temperature over the left lower extremity is attributed to vasoconstrictor action.

Curschmann,² also, accepts the possibility of an intermittent claudication with apparently intact (?) arteries, where the symptoms are referable to a genuine constriction of the pedal arteries. In two females (between the ages of 19 and 22) he found the typical manifestations associated with *absence* of the pulses of the feet and *without* any evidence of arteriosclerosis. He claims that such instances are analogous to the intermittent asphyxia of the hands, differing in that the pulses are permanently absent in the former.

It is, however, just this constant lack of beat in the pedal vessels that throws considerable doubt on the accuracy of his observations. A permanent arterial spasm is so foreign to analogous conditions elsewhere, that our mental approach to such a possibility can hardly divest itself of the suspicion that a true organic obliteration did exist.

Relation of Angiospasm to the Organic Type of Intermittent Claudication.—We have purposely retained here the designations, angiospastic (neurogenic or vasomotor) and organic intermittent claudication (dysbasia angiosclerotica—Erb), in order to express more clearly the views of the authorities who have employed these terms. For it must be borne in mind that amongst a large number of the continental observers, the conception of the malady "intermittent claudication" had taken root so strongly, that, with the discovery of diverse, contradictory and inconsistent physical findings, in arteriosclerotic arteries (Erb), in acute arteritis (Higier), in obstructed arteries (Higier), and with patent arteries (Oppenheim's angiospastic form), a confusing collection of clinical descriptions had found their way into the literature. To clarify some of these notions, reference must be made to theories according to which vasomotor neuroses are regarded not only as the antecedents, but also as actual harbingers of organic vascular changes in a causal sense.

¹ Rülf, Arch. f. Psychiat., 56, H. 1, p. 899.

² München. med. Wchnschr., 1907, No. 51, p. 2522.

Oppenheim entertains the belief that the angiospastic neurosis with symptoms of intermittent claudication may be a prodromal stage of what he terms organic intermittent claudication or "dysbasia angiosclerotica." In defense of this proposition he cites a case of a young man in whom vasomotor manifestations preceded by years, the final appearance of intermittent claudication with evidences of arterial obliteration.

H. H., male, 28 years, gave a history of neuropathic tendency, insomnia, frequent attacks of "dead fingers," and even local syncope in these, with sensation of "pulsations" in various parts of the body, with excessive sexual irritability. The feet showed nothing abnormal (February, 1895).

Two years previously after emotion, he had pain with coldness in the calf of the legs on walking 1 to 3 minutes, necessitating a pause before further progression was possible. After lasting about a year, these symptoms disappeared.

In 1899, a recurrence of difficulty in walking, with the right leg especially affected, was noted. The plantar aspect of the toes of this limb would become pale with slight cyanosis after fatigue. The corresponding dorsalis pedis artery could not be felt pulsating.

In 1911 the pulses of the right foot were altogether absent, present on the left. Coldness and cyanosis were also striking signs. Pain and cyanosis appeared after walking 30 to 40 steps. X-ray examination showed distinct calcification.

In short, evidence has been brought forth, at least in this case, that the phenomena of intermittent claudication *may coexist with pulsating vessels* in a neurotic individual with other stigmata of a labile vasomotor system; that, later, such a patient may, after free intervals, pass over into a stage in which the peripheral arteries are arteriosclerotic and obturated. While such a chronological sequence of events doubtlessly may occur, the causal relationship between the stage of angiospasm and the subsequent development of organic disease, be this arteriosclerosis, thrombo-angiitis obliterans, or thrombosis, is not so clear. To conceive of peripheral thromboses as a complication during the history of repeated attacks of vasomotor constriction, is logically permissible, and, certain observations of the author would support such an assumption. An analogous condition obtains in cases of gangrene in anatomically normal arteries and in the cases of thromboses in peripheral arteries without arteriosclerosis or other disease.¹ In some of these acrocyanosis had been noted although intermittent claudication was usually absent.

But to assume, as does Oppenheim, that there is an intimate motivating dependency between a prior neurotic status and a succeeding arterial disease, would appear an audacious hypothesis, in light of the fact *that in that most intense and exquisite form of angiospastic condition, Raynaud's disease, such an organic vascular eventuality is altogether lacking.*

A perplexing situation, diagnostically speaking, will not infrequently confront us, one that may be interpreted as reliable testimony in favor of Oppenheim's belief. This is the circumstance that marked vasomotor symptoms, occasionally with, but usually without intermittent claudication may occupy the clinical picture, weeks, months, or almost years before the typical objective manifestations of thrombo-angiitis obliterans are recognizable. References to this type will be made in Chap. LIX.² To deduce a causal association between the excessive lability of the vasomotor functions and the consequent inflammatory and obstructive vascular lesions, would, in our opinion be unwarranted.

Whenever pronounced neurotic vascular symptoms participate in the early stages of an insidiously developing organic obstructive arterial lesion, we must consider the following possibilities.

¹ See Chap. XCVIII.

² See Vasomotor Symptoms in Thrombo-angiitis Obliterans of the Upper Extremities, and also Chap. "Borderline Cases" CIV.

First, two independent diseases may overlap, coexist or follow each other.

Second, minimal unrecognizable peripheral vascular obturating processes (as in thrombo-angiitis obliterans of the plantar arteries or peripheral pedal vessels) are present for a long time, and are a factor, not only in evoking the cyanosis or pallor of the digits on exertion, but also secondarily elicit a superabundant quota of vasomotor response; and this, either by virtue of the superfluity of waste products (toxins, CO₂, etc.) developed in poorly nourished territories, or by a relative ischemia when the circulation is impaired.

Third, thromboses of the popliteal artery of clinically unobserved, stealthy advent, with adequately dilated collateral paths filling the dorsalis pedis and posterior tibial arteries may be accountable for a complex that is wont to be diagnosed as a vasomotor form of intermittent claudication.

A more complete exposition and an analysis of this subject are given in the section on the critique of so-called angiospastic forms of intermittent claudication also in Chap. CIV.

While Oppenheim lays great stress on two factors, namely, a neuropathic and an angiospastic diathesis, as being important in intermittent claudication, he seems to have overlooked the possibilities above mentioned. Higier, himself, to whom he oft refers, was not clear as to the pathology of most of his cases. Amongst the latter's cases can be recognized exquisite examples of thrombo-angiitis obliterans in the chronic or in the acute relapsing stage. Just how important are the other predisposing moments to which Oppenheim alludes, to wit, the congenital Anlage or congenital mediocrity or inferiority of the vascular and nervous systems, it is impossible to say.

In short, this author recognizes a "genuine" or true organic form of intermittent claudication and an angioneurotic. But even for the former variety he would postulate the existence of a congenital mediocrity or inferiority of the vascular system, a degenerative stigma that runs parallel with the neuropathic diathesis of these individuals. The finding of abnormally small femoral arteries *in vivo* during their exposure for the performance of the Wieting operation of arteriovenous anastomosis, convinced him of the correctness of his hypothesis.

III. INTERMITTENT CLAUDICATION IN OTHER TERRITORIES

In fact a number of authors have observed phenomena attributable to occlusive conditions in the arteries of the affected parts, and Ortner¹ described what he calls:

(a) Dyspragia Intermittens Angiosclerotica Intestinalis.

In a male 55 years of age, an inveterate smoker, there were attacks of pain in the umbilical region 2 to 3 hours after a large meal, the symptoms lasting 2 to 3 hours. For several months there would be periods of intermission with recurrences. Exitus occurred after an operation.

Autopsy showed marked atheroma of the aorta, the superior and inferior mesenteric arteries being markedly sclerotic. There was nothing else to account for the symptoms.

Determann described a case of intermittent claudication, involving an arm, one lower extremity and the tongue. This latter case, however is open to the criticism that there were not multiple arterial obturations, but that some of the cerebral arteries were involved.

(b) **Intermittent Claudication of the Spinal Column.**—Even an affection of the vessels of the spinal cord has been described by Déjerine,² who men-

¹ Ortner, Wien. klin. Wchnschr., 1902, p. 44.

Ibid., Volkmann's Vorträge, N. F., 347, Leipzig, 1903.

² Déjerine, Rev. neurol., 1906, 14, p. 341.

tions in the clinical picture an onset with cramp-like contracting sensations of heat and cold in one or both legs brought on by walking and disappearing after repose. With this, gradual aggravation of the symptoms, weakness after the slightest exertion become so accentuated that the legs are practically functionally useless. Paralysis and evidences of contracture are absent. Increased reflexes and ankle clonus appear during the attack, as well as the Babinski reflex. Urinary and sexual disturbances may be associated, although sensory phenomena are absent.

The histories reported by Déjerine¹ describe cases in the third or fourth decades with lower extremities that show no disturbances when in repose. After a short walk the limbs become heavy, motion more and more impaired until locomotion becomes impossible. Motor power returns after a few minutes of rest. Parasthesia, cramp-like sensation, formication, coldness and heat may be associated and also disappear during the period of rest.

At the onset of this disease the patient must pause but rarely, being able to walk considerable distances, possibly even a mile, but later on the patient may require a rest after twenty or thirty steps.

An ankle clonus, occasionally also a Babinski sign, that are absent, during rest can be elicited after motion. Occasionally urinary frequency and urgency and sexual hyperexcitability are associated symptoms.

At the same time one can demonstrate all evidences of pathological alterations in the vessels; the pulses are present and also the vasomotor manifestations that usually accompany intermittent claudication.

The prognosis is bad in these cases since a spastic paraplegia eventually develops. This outcome speaks for the assumption that an organic alteration is responsible for this affection.

Déjerine believes that there is a deficient circulation in the dorsal portion of the lumbar cord by reason of a chronic arteritis. In all probability the permanent changes in the cord do not develop until a long period has elapsed since the history of the cases is long with marked remission in the symptomatology.

Other authors, such as Grasset² and Sollier³ have confirmed the above observations. In contradistinction to the two forms of dysbasia and angiosclerotica intermittens, syphilis probably plays the most important part in determining endarterial lesions in the cord.

Other authors, amongst whom Hardy,⁴ Long,⁵ and Rekord,⁶ may be mentioned, have made similar observations.

(c) Intermittent Claudication of the Upper Extremities.—The upper extremities may be the seat of similar phenomena.⁷ The author has described their occurrence in thrombo-angiitis obliterans as well as in arteriosclerotic lesions of the vessels.

A number of cases have been reported in which the complex, intermittent claudication, involves both upper and lower extremities, with absent pulses in both. Whilst in some of these the findings would point to atherosclerotic vessels, in others the data given are not conclusive.

¹ Déjerine, Thèse Paris, 1894, p. 179.

² Grasset, S., Rev. neurol., 1906, XIV, No. 10, p. 433.

³ Sollier, Presse med., Oct., 1906, No. 85, p. 677.

⁴ Hardy, Thèse de Paris, 1909.

⁵ Long, Rev. med. de la Suisse romande, 1910, p. 7.

⁶ Rekord, Amer. Jour. Med. Sc., 1912, 114, p. 721.

⁷ Buerger, *Loc. cit.*

In the case of a man 58 years of age (Tobias¹) symptoms were present in both lower extremities and in the *left arm*. In the legs, there was a feeling of coldness and pain in the calf muscles upon walking, and for 1 year similar manifestations in the left arm. Striking was the early fatigue occasioned in the latter after using it. The intense feeling of coldness of the left hand necessitated the wearing of heavy gloves.

Physical examination showed an absence of the dorsalis pedis and posterior tibial pulses of both lower extremities; in the left upper, the axillary and subclavian pulsated, whilst *all other large pulses were absent*.

Determann employs the term *dyskinesia intermittens angiosclerotica* to which the adjectives *cruris* and *brachii* are added for the leg and arms respectively.

In a case of Nothnagel (1867) there was a thrombotic occlusion of the right axillary artery.

In an arteriosclerotic woman of 25 the right axillary artery had been converted into a hard cord, easily palpable in the axilla and below this. The pulsation in the radial artery was absent, and in the ulnar and brachial there was but a slight beat. When the girl used the right arm even for the lightest kind of work, weakness soon resulted, with pain and paresthesiæ in the hands and fingers. Work became impossible; after rest it could be begun again. It was not clear as to how the thrombus had developed in the artery. A somewhat insufficient collateral circulation had resulted.

Whilst in the above-mentioned case extensive vascular disease was not present, but a localized thrombotic process was held responsible for the impaired circulation, other instances are reported where one or both upper extremities were involved in a manner similar to that of the lower extremities.

In a case of Wedensky² the right arm was involved as follows:

A male 38 years of age was suffering from intermittent claudication of the right leg, with symptoms also in the right arm. He could not write for any length of time without experiencing pain in the fingers and also in the wrist. At the same time there was hyperhidrosis and later coldness of the whole right arm. In moderately cold weather the wrist and fingers would get blue. There were periods of improvement and intensification of the symptoms, until finally ulcers appeared on the second and third fingers, which, however, healed under treatment. At about this time gangrene of the third toe of the right foot occurred, necessitating exarticulation of the toe.

Examination revealed the fact that the right arm was somewhat atrophic and colder than the left, and that the pulses in the right radial and ulnar arteries were absent.

As a rule the symptoms in the upper extremities are associated with similar symptoms in the lower. Up to the year 1907, Bing was able to find about one dozen cases described in the literature.

An interesting case is reported by Determann³ where the tongue also gave symptoms.

A Russian (Hebrew) who smoked 6 cigarettes a day complained, in addition to the usual symptoms in a leg and arm, of the following, very annoying manifestations: after speaking from 5 to 8 minutes, the mechanical act of articulation was impaired, although no interference with the mental functional mechanism was present. Gradually the tongue would become heavy and thick, motility returning after a short period of rest. The examination of the lingual pulse revealed bilateral weakness.

IV "ACUTE"⁴ FORMS OF INTERMITTENT CLAUDICATION

An inchoate, unreliable and unsatisfactory classification has resulted from the trend of a number of excellent observers to accentuate the importance of the symptomatic association called intermittent claudication, and

¹ Tobias, Ztschr. f. d. ges. Neurol. u. Psychiat., 1921, 71, 309.

² Wedensky, Langenhecks Arch. f. klin. Chir., 1898, LVII, p. 98.

³ Determann, Deutsch. Ztschr. f. Nervenhe., 1905, XXIX, p. 152.

⁴ "Acute" in quotation marks since this is an appellation of other authors.

also from a neglect of the pathologic basis or true morbid process. Some time prior¹ to such reports as to those of Higier² the author had already studied vascular material from identical cases, and had been able to recognize a clinical and pathological entity, to which the designation thrombo-angiitis obliterans had been given. Intermittent claudication was regarded as one of the manifestations of occluded arteries accompanying this as well as other maladies.

The acute form of intermittent claudication of other authors corresponds to two essential vascular lesions; first, to the acute stage of thrombo-angiitis obliterans with sudden extension of the inflammatory and thrombotic obturation over varying territories; and second, to the deposition of keystone, parietal or even completely obliterating thrombosis in arteriosclerotic vessels.

(a) **Acute Stage of Thrombo-angiitis Obliterans.**—The contributions to the literature of "acute intermittent claudication" have added considerably to the clinical confusion already sufficiently ingrained and impressed by multitudinous and variant descriptions of types of intermittent claudication. Whilst Higier³ reports a clinical picture of subacute or chronic course as intermittent claudication or angiosclerotic paroxysmal myasthenia in one publication, he speaks of "arteritis acuta with intermittent claudication" elsewhere,⁴ when the onset of the malady is sudden. In the former⁵ he was, we believe, dealing for the most part with cases of thrombo-angiitis obliterans of the chronic progressive type; in the latter, with the same malady during a period of acute manifestations. In neither instance, was this author justified in speaking of a disease "intermittent claudication."

The case of Higier⁶ reported in 1910 corresponds with the author's "acute stage" or acute thrombotic exacerbation in thrombo-angiitis, and can in no sense be regarded as a rarity. He cites the following history.

A Polish Hebrew, 25 years of age was suddenly seized with pain in the right foot. Fever, chills and general depression *were absent* at the onset, and there was no local swelling, abnormal redness or heat, abnormal pallor, cyanosis or coldness. Examination of the internal organs was negative. There was no increased blood pressure and no anemia. The urine was free of albumin and sugar. Intense pain in the right foot and leg made walking impossible, but abated with the patient in bed and at rest. Walking, even after some 30 or 40 paces, produced a feeling of numbness and fatigue in the calf of the leg, necessitating immediate cessation of locomotion. A certain degree of pallor of the foot seemed to follow repeated or prolonged movements of the extremity, whereas the pendent foot turned to a livid or rose color (erythromelia). The temperature of the extremity was lowered. The right dorsalis pedis and posterior tibial arteries did not pulsate. Later, exceedingly painful ulcers of the second and third toes developed. Radiography showed no arterial calcification. The pulses of the leg were present. In the past history nothing of moment could be elicited, no lues, no exposure to cold nor to trauma.

The insomnia which did not respond to sedatives and hypnotics *made the patient desperate and he was anxious to accept the physician's proposal of amputation*. However, after three months the ulcers healed, and the pain as well as the intermittent claudication diminished greatly. Six weeks later he was able to get up.

The physical examination made about ten months after the first symptoms, showed persisting coldness, moderate lividity of the foot, and absence of the pulses.

In the light of the author's⁷ studies, and in a comparison with almost identical observations in which pathological material through amputation

¹ Buerger, Amer. Jour. Med. Sc., Oct., 1908; Proc. New York Path. Soc., March, 1908.

² Neurol. Centralbl., 1910, p. 911.

³ Higier, Deutsch. Ztschr. f. Nervenhe., 1901, XIX, p. 439.

⁴ Higier, Neurol. Zentralbl., 1910, XXIX, p. 911.

⁵ See "Intermittent Claudication," p. 255.

⁶ Higier, Neurol. Centralbl., 1910, XXIX, p. 912.

⁷ Buerger, see literature on Thrombo-angiitis obliterans.

was available for study, there can hardly be any doubt but that the case reported by Higier was one of thrombo-angiitis obliterans. That extensive acute inflammatory thromboses occur throughout the territory of the dorsalis pedis, posterior tibial, peroneal and popliteal arteries in thrombo-angiitis obliterans, the author has demonstrated beyond the shadow of a doubt. And, the manifestations called forth correspond in almost every detail to those in the story above related.

How misleading an attempted grouping of unrelated diseases under the caption "Intermittent claudication" can be, is well illustrated both by Erb's quest for a special category in which to put the so-called "acute form of intermittent claudication," and Higier's renewed necessity for separation of his "angiosklerotische paroxysmale Myasthenie" from the "acute type" subsequently called "arteritis acuta with intermittent claudication."

(b) Arteriosclerosis with Thromboses Diagnosticated as Acute Intermittent Claudication.—Elsewhere will be described a characteristic picture of "acute attacks of thrombosis" in cases with arteriosclerotic vessels (Chap. LXIX). In some of these intermittent claudication has preceded by many months or years; in others, *no* clinical evidence of vascular affection has made itself manifest. When, therefore, a patient with no past history referable to the lower extremities, suddenly develops intermittent claudication or other phenomena resulting from vascular occlusion, *a thrombotic lesion is the most probable cause*, although palpatory evidences of such occurrence may be absent. Cases such as that reported by Pelnar¹ may be classified from the pathologic standpoint as latent arteriosclerotic vascular lesions with secondary parietal and occlusive thromboses. The history report may be summarized thus:—

An engineer, 61 years of age, developed the following symptoms rather rapidly. After walking but a few (2 to 3) steps he experienced a peculiar uncomfortable sensation in the whole left lower extremity, as if the limb were foreign to him, this feeling gradually giving way to heaviness and lack of control of the affected part. This necessitated pausing to rest, immediate recurrence of these manifestations following renewed attempts to move about. So severely was he affected that only the most necessary steps were taken, the sitting posture offering considerable relief.

His wife noted that his toes would be cold, pale and "like dead," the left leg colder than the right. Because of tenderness in the left groin, the respective region was protected from all pressure and contact. There had been a previous history of mild apoplectiform attack with recovery.

Physical examination November 5, 1909, revealed increased blood pressure (180 mm. systolic) generalized arteriosclerosis, and cardiac enlargement. The femoral artery below Poupart's ligament was tender and its pulsation weaker than that of the other side. The left dorsalis pedis beat was also diminished.

Iodides were administered and in 1 month the subjective symptoms abated considerably, and walking became easier. So also the tenderness in the groin became limited to a small area. Objective signs remained stationary and the blood pressure rose to 210 mm. (systolic).

In August, 1910, he was again seen and found to be suffering from the results of an apoplexy whose onset was recorded as January, 1910. The right side was the seat of slight paresis. The symptoms in the *left* lower extremity were noticeable only after prolonged exertion and locomotion, and were of only moderate degree. The left femoral and popliteal beats were weak, whilst the dorsalis pedis artery could "hardly be felt."

In short, a case of marked arteriosclerosis, high blood pressure, apoplectiform attacks, with rather sudden advent of enfeebled pulsations, the arterial distribution of the left lower extremity being accompanied by the usual symptoms of intermittent claudication with gradual improvement and practical disappearance of the dorsalis pedis pulse. Such examples have frequently

¹ Pelnar, Neurol. Zentralbl., 1911, XXX, p. 9.

been observed by the author, and when gangrene eventuates—as occurs in a certain percentage of the cases—the existence of thrombosis superimposed upon the arteriosclerotic lesion has been demonstrable at autopsy or dissection of the amputated limb.

Doubtless parietal, keystone, and completely occlusive thrombi are responsible for similar clinical pictures. *Syphilis* also, and still unknown forms of *arteritis*—(thrombo-angiitis obliterans being a distinctive, well differentiated type), by virtue of complicating thrombosis and obstructive impairment of the circulation can give rise to like symptom-complexes.

V. APOKAMNOSIS (GOLDFLAM¹) OR ARTIFICIAL INTERMITTENT CLAUDICATION

Goldflam employed this term to denote abnormal liability to fatigue in myasthenia, and transferred its application so as to designate also a feeling of tiredness, numbness, heaviness and tension evoked by actively lifting the affected limb. Whilst these manifestations can be artificially induced in an extremity in which intermittent claudication occurs, in the normal only slight pain or a feeling of fatigue will be tardily produced. Latent cases of intermittent claudication may be brought to light by this test—instances in which the typical signs have not as yet developed—and in which pallor, rubor and cyanosis may dominate the clinical picture. As a comparative method of investigating two corresponding limbs, it may reveal sufficient differences to be of diagnostic worth.

Artificial pallor is also producible in cases with symptoms of intermittent claudication, if the foot—whilst in the horizontal position—be flexed and extended some thirty to forty times. The color contrast is even more strikingly forthcoming, if the leg be permitted to hang down when the exercises are carried out. Blanching of the fingers and hand can also be made to occur by repeated flexion and extension of the fingers with arms hanging. But most noteworthy is the ischemia of the foot following walking, particularly if a test of locomotion be tried after the patient has been standing for some time.

Goldflam attempts to explain the cutaneous ischemia in the following manner. With the active motion of the extremity and the implied muscular contractions, a hyperemia of this territory with dilatation of the arteries occurs. With this “functional hyperemia” of the muscular vessels, a collateral cutaneous anemia is to be expected. Invoking also the participation of the vasomotor nervous system, he calls attention to the autonomous self-regulating mechanism that is an inherent rôle of its activities, so that with the necessary dilatation of the deep arteries a corresponding constriction of the capillaries and arterioles of the integument, is an essential compensatory sequence.

PATHOLOGY

A study of the literature is exceedingly unsatisfactory, because of the fact that authors have not differentiated between the obliterating lesions of arteriosclerosis those of so called “endarteritis obliterans,” and the obturating process of thrombo-angiitis obliterans. The failure to properly interpret the histological picture resulting from the canalization and vascularization of obturating thrombi has produced confusion in the literature; no cognizance having been taken of that special, inflammatory and thrombotic

¹ Goldflam, Neurol. Zentralbl., 1910, XXIX, p. 2.

lesion described by the author. In fact, the lack of distinguishing criteria between arteriosclerosis, endarteritis obliterans and thrombo-angiitis obliterans, has permitted an incorrect conception of the pathology of these conditions to persist.

Thus, the cases of Charcot, Dutil and Lamy,¹ Laveran,² Panas,³ Goldflam, Erb, and others are described by authors who have made a critical study of their publications, as examples of a productive or obliterating endarteritis. Endarteritis obliterans in this sense is considered to be a progressive thickening of the intima, through proliferation of a cellular, new-formed connective tissue, leading to complete closure of the arterial lumen.

This interpretation is incorrect, for, some of the cases mentioned are examples of arteriosclerosis, others of syphilitic endarteritis, and still others of thrombo-angiitis obliterans.

Bing⁴ in his resumé of intermittent claudication is unable to differentiate between endarteritis obliterans of Friedländer—which in all probability is identical with thrombo-angiitis obliterans—and that of arteriosclerosis. Be that as it may, it can be gleaned from the literature, that in spite of uncertainty as to the exact pathological nature of the obstructive arterial conditions observed, most authors are in accord in the opinion that organic impoverishment of the circulation by an obturating vascular affection is usually the pathological substratum.

In the consideration and treatment of the subject of etiology and pathogenesis, the lack of proper recognition and segregation of types of pathological process have also entered into the production of inexplicable and conflicting statements and circumstances on the parts of various authors. It can therefore be readily understood how the views of one observer who described only the arteriosclerotic form of intermittent claudication can be diametrically opposed to those of another author dealing with cases of thrombo-angiitis obliterans, as to the question of the particular age at which the process is most apt to occur. In the former, older individuals, in the latter the young, and predominatingly the Hebrew race will be affected. It is just this inability to differentiate between the types of cases that has called forth much academic discussion and many controversial argumentative publications.

Causal agents of varied nature such as chemical toxins, static, and even neurotic influences have received the attention and recognition of commentators on this subject.

According to one set of statistics regarding age (Erb), there were but 3 cases under 30 years; from 30 to 40, there were 9; from 40 to 50 years, 20; from 50 to 60 years, 27; and from 60 to 70 years, 14 patients. So the largest number occurred between 40 to 60, the age at which arteriosclerosis is most pronounced.

Some authors report cases in even young individuals. Higier⁵ and Idelsohn⁶ cite such cases in young people, the latter also referring to a patient 34 years of age. Some of these were doubtlessly cases of *thrombo-angiitis obliterans*. Indeed, Higier concludes that of his 23 cases at least one-half were under the age of 40.

¹ Dutil and Lamy, Arch. de méd. exper. d'anat. path., 1893, p. 102.

² Laveran, Acad. de Méd. Séance du 27 fév., 1894.

³ Panas, Acad. de Méd. Séance du 5 juin, 1894. Sem. méd., 1894, p. 265.

⁴ Bing, Beiheft z. med. Klin., 1907, p. 117.

⁵ Higier, *Loc. cit.*

⁶ Idelsohn, Deutsch. Ztschr. f. Nervenhe., 23, S. 285.

The affection occurs more frequently in men than in women, and according to Erb there were but 9 cases in females amongst his 168 cases. The Hebrew race is said to be particularly predisposed, as well as the inhabitants of East Russia, Poland, the Baltic Provinces and Finland.

Excessive use of tobacco is cited by Erb as one of the most important causal factors, and he gives the following statistics:

Of 500 males taken from the better classes, who did not present the symptoms of intermittent claudication, 4 classes could be distinguished according to indulgence in tobacco (smoking), as follows:

Non-smokers or almost non-smokers; a second class of moderate smokers (3 to 6 cigars or 10 to 15 cigarettes); a third class (7 to 12 cigars or 15 to 40 cigarettes); and the fourth class of excessive smokers (40 to 100 cigarettes). Of the 500 males, 44.8 belong to the first class, 31.6 to the second, 17.8 to the third, and 5.8 to the fourth. Of the cases of intermittent claudication, however, 7 per cent belong to the first class, 14 per cent to the second, 50 per cent to the third, and 28.6 per cent to the fourth. From these statistics one may conclude that there is a preponderance of smokers amongst patients suffering from intermittent claudication.

Idelsohn attached some importance to the existence of flat feet in certain cases. Determann observed a hereditary tendency to arteriosclerosis in one family, and a neuropathic or neuro-angiospastic disposition is held by others to play a significant rôle.

A neuropathic habitus is regarded by Oppenheim, Erb and Goldflam, as of some importance as a contributing etiologic factor. Its frequent incidence in Hebrews and the coexistence of hereditary psychoses, congenital anomalies and functional neuroses have given weight to this view. Oppenheim has suggested that an angiospastic disposition is not uncommonly associated with intermittent claudication, and further inclined to the hypothesis that a congenital narrowness of the arterial system may be in some way related to such vasomotor inclination.

In another publication Erb concludes that intermittent claudication corresponds in the age at which it afflicts individuals with the period during which arteriosclerosis is most apt to occur. A preponderating number of his cases was over 40 years of age. Of 57 cases only 1 was under 30 years; between 30 and 40 there were 8; between 40 and 50 there were 19; between 50 and 60 there were 20; and over 60 years there were 9 cases.

Higier (whose views have been considered elsewhere) and who undoubtedly had for the most part cases of thrombo-angiitis obliterans under observation, reported that of 23 cases, 50 per cent were under 40 years of age.

The mere fact that the intermittent claudication described by all of these authors is extended to include the totality of symptoms in a number of different pathological processes, and in the case of Erb said to be connected with arteriosclerosis of the vessels of the lower extremities, and in the case of Higier to correspond to the disease, thrombo-angiitis obliterans—is sufficient argument in favor of the view oft expressed by the author, that associated symptoms common to a number of different lesions and morbid processes must not be exalted into the equivalent of the morbid processes themselves.

Had some of these observers the opportunity of being convinced of the absolute pathologic differences that underlie the vascular obturation in the various cases, their classification would in all probability have been carried out on a pathologic rather than on a clinical foundation.

The circumstance that the symptoms of intermittent claudication may be absent in cases of outspoken arterial disease, suggests the importance of a functional factor—an angiospastic condition—as responsible for the symptoms. So Erb concludes that the necessary vasodilatation that normally is a concomitant of increased function is absent in these cases, and even accepts the possibility of vasoconstriction in the pathologically changed vessels. So

also is Bing willing to agree in this assumption basing his view upon the significance of the ischemia and cyanosis of the skin—phenomena dependent upon vasomotor action.

We shall discuss these matters critically in another section, and it may suffice here to say that whilst these views may be correct in part, they lack foundation insofar as vasoconstriction of the obliterated vessels is inconceivable. However, that an additional moment, namely, a vasomotor process is active in other vessels, that is, in the normally patent vessels, be they of the skin or of the subcutaneous tissues, or uninvolved muscular vessels, is not only possible, but undoubtedly takes place. It occurs in two types of cases.

Firstly, in cases in which the symptoms of intermittent claudication are dependent upon and associated with marked obliteration of some or many of the large vessels and

Secondly, cases in which the patency of the larger vessels is unimpaired.

CRITICAL SUMMARY

When described as a clinical entity by certain authors (Higier, Idelsohn, Kahn, Köhler), the symptomatology will be found to correspond to pathologic processes of different nature and to be inclusive not only of thrombo-angiitis obliterans, arteriosclerosis of the vessels of the extremities, but also of certain vasomotor affections of doubtful nature. Let us summarize the symptomatic history as described by these and other authors, so as to illustrate most vividly the misconceptions that such a grouping will create. Then only will the fallaciousness and incoherency of a mere clinical association of wholly unrelated morbid processes, be well appreciated.

Thus Cassirer¹ summarizes *the course of intermittent claudication* as follows:—"The malady (intermittent claudication) usually takes a chronic course, although the severe symptoms may arise rather suddenly. Prodromal signs are usually to be observed. The symptoms, the paresthesiæ, pain, tension, gradually increase to the severity of well marked intermittent claudication that materially interferes with occupation."

In this very first descriptive paragraph, the simultaneous usage of the appellation, intermittent claudication, both as a noun and as an attribute or adjective, is illuminating. Then follows:—"If now, an arrest cannot be brought about through correct therapy and diet, progressive gangrene of the toes, of the foot or of the leg with the usual severe consequences, is the issue. Sometimes a stationary period intervenes after gradual improvement; an adequate collateral circulation may be developed or the arteriosclerosis may abate."

Such a clinical picture is no more applicable to intermittent claudication than it is to any of the other striking phenomena of obstructive vascular disease of the extremities. It corresponds to arteriosclerosis, as well as to thrombo-angiitis obliterans and other types of thrombotic lesion. By the same token, and by similar reasoning, *rubor* or erythromelia, or *ischemia*, mere manifestations, may be elevated and exalted into the rank of separate maladies. For both of these examples, mentioned to illustrate by analogy, are just as frequent concomitants of obstructive arterial processes as is "intermittent claudication."

¹ Cassirer, *Loc. cit.*

The pathognomonic evidence of intermittent claudication is termed "paroxysmal myasthenia" by Higier.¹ He describes the typical phenomena just as Erb and Cassirer have, and adds that for diagnostic purposes, the coincidence of weakness or absence of pulses in the affected territories is an essential accompaniment of the paroxysmal recurrent dysbasia. He, too, therefore, accepts an anatomical pathological substratum in the arteries as the basic lesion.

Indeed, a study of Higier's article² on "Angiosclerotic Paroxysmal Myasthenia (claudication intermittente of Charcot) and Spontaneous Gangrene" will engender the conviction in any observer conversant with the disease thrombo-angiitis obliterans, that the latter malady and not intermittent claudication had come under that author's observation. Although he recognized the existence of a vascular affection in his cases, a lack of pathological material is responsible for his view that a neuropathic diathesis plays the most important rôle in the symptomatology. Conceding to functional neurotic factors a preponderating influence in the clinical manifestations, he nevertheless recognizes the existence of arterial disease and secondary nerve degeneration. That his own conception of the interrelationship between arterial affection and intermittent claudication is discordant and at variance with the author's is to be gleaned from his belief that *the vascular processes are secondary in some cases to a primary nerve lesion*.

EXPLANATION OF PHENOMENA

Many explanations have been given to account for the symptoms induced by exercise, most authors invoking a vascular spasm as the most plausible.

Such vasoconstriction would be pathological, since our physiological concepts presuppose dilatation as a response to excessive demands. Some assume that an abnormal vasoconstriction or reflex is the reaction of pathological arteries. This view is, however, not altogether satisfactory, firstly because the diseased vessels in blocked territories (such as thrombo-angiitis obliterans) must surely have lost their contractile powers, and secondly, since the more peripheral disturbances in the supplied muscles and other tissues are then not taken into account as a possible source of origin for special or abnormal reflexes.

Intermittent Claudication with Healthy Arteries.—Zak has shown³ that identical symptoms are producible after exercise in a normal upper extremity when the brachial artery is artificially compressed.

If the brachial artery be compressed with the finger with the arm in a horizontal position, and then repeated opening and closing of the hand be carried out some 30 or more times, increasing weakness and fatigue set in; on further motion a cramp-like sensation appears in the hand up to the wrist, and later such pain as to make flexion and extension impossible. Simultaneously a cadaveric hue of all five fingers develops, which is limited about at the metacarpal phalangeal level, or extends somewhat up the dorsum of the hand. Sometimes the pain extends up to the elbow, together with a sensation of fatigue.

When the blood is allowed to enter again, a typical red hyperemia (reactionary) takes place over the arm and hand, but the pallor of the fingers may persist for 10 or more seconds, yielding gradually to pale pinkish or rose colored patches.

This experimentally or artificially induced symptom-complex is comparable to that of intermittent claudication, and can be demonstrated to occur

¹ Higier, H., Zur klinik d. angiosklerotische paroxysmalen Myasthenia, etc., Deutsche Zeitschr. f. Nervenheilk, 1901, 19, pp. 438-466.

² Loc. Idem.

³ Zak, Wien. Arch. f. inn. Med., 1921, 2, p. 408.

with vessels altogether healthy. Explanations for the genesis of the phenomena, other than reflexes emanating from the diseased vessels themselves, therefore must be resorted to.

Not only can the sensory manifestations of intermittent claudication be stimulated in the above way, but data seem to indicate that in an ischemic limb, conditions are at hand which predispose to angiospasm or heightened vasoconstriction of the small vessels as the result of exertion.

And so it has been observed that whereas the resting limb will react (reactionary hyperemia) in a sudden fashion upon the release of an Esmarch bandage or compression of a main nutrient artery, a considerable delay of this vasodilating response, and a persistence of vasoconstriction occur, if such an artificially ischemic limb be allowed to exercise. From this it has been concluded that a state of vasoconstriction or spasm in a multitude of vessels in the ischemic vascular territory, responding in this heightened way to exercise, may be responsible for the symptom-complex, intermittent claudication.

Theories as to the Cause of the Angiospasm.—More recent views tend to the acceptance of a chemical or chemiconeuro reflex explanation. When the main artery of a limb is compressed or an Esmarch bandage or a tourniquet is applied, a consequent ischemia or anemia depends not only upon a lack of blood in the arterioles and capillaries, but also upon arterial constriction. This is demonstrated by the author as obtaining in thrombo-angiitis obliterans upon elevation of the affected extremity. The small vessels do not collapse in their true sense, but contract—possibly a functional response or defense against reflux or venous blood. Indeed, Hering concludes that venous blood exercises a vasoconstricting influence on the arterial wall.

The Rôle of Chemicals in an Anemic Territory.—Many other data¹ discovered by physiologists have disclosed the influence of chemicals on the contractility of the smaller blood vessels. Fleisch² showed that weak concentration of carbon dioxid causes vascular dilatation, whilst strong concentration causes contraction. Dearth of oxygen causes vasoconstriction. Thus, it has been assumed that the diminution of oxygen may be responsible for vascular constriction. Not only a direct chemical effect upon the arteries has been thus revealed, but even an indirect vessel reflex through nervous influences was demonstrated by the author; for similar contraction was produced in territories only in nerve connection with that in which carbon dioxid accumulation has been experimentally produced.

Therefore, two antagonistic reflexes may be at play in a member, whose circulation has been put in abeyance but allowed to exercise; firstly, the normal vascular dilating reflex of a functioning part with normal circulation; and secondly, a vasoconstricting one, which is especially active in the badly nourished territory. In the latter accumulation of carbon dioxid or deficiency in oxygen may account for the abnormal reflex. When the constricting influence overbalances the dilating, the subjective and objective phenomena of intermittent claudication may be produced. In the presence of increased carbon dioxid concentration and deficiency in oxygen, a normal vasodilating response is diminished or put in abeyance. This is the theory advanced by some of the more recent observers.

More recent work (Hopkins³) emphasizes the importance of the development of lactic acid in muscle physiology. The prime, if not the sole, cause of fatigue in muscle is believed to be the accumulation of this acid. Although the author has been unable to find any investigations of illuminating nature regarding the direct effects of lactic acid in evoking a vasoconstrictor reflex action, the general trend of interpretations seems to regard the deficiency of

¹ See Capillary Circulation.

² Fleisch, Pflügers Arch., 1918, Bd. 171.

³ Hopkins, Harvey Lectures, April 2, 1921 (Lippincott).

oxygen and the accumulation of acid waste products as responsible; lactic acid would be one of these.

Whether failure to eliminate lactic acid and the consequent change in the elastic properties of the muscles may be translated into a direct response in *sensory nerves*, without implication of vasomotor mechanism, is another hypothesis worthy of consideration. It would presuppose a direct analogy between the cramp-like pain of excessive fatigue in healthy, well nourished tissues, and the symptoms of intermittent claudication, both explicable in the light of the above theory.

DIFFERENTIAL DIAGNOSIS

1. *Myasthenia Gravis Pseudoparalytica*.—In this affection, too, we also note an intermittent disturbance of motor function that returns with each and every exertion, but is distributed over wide muscle territory, is characterized by a typical electrical reaction, and is unaccompanied by sensory or vasomotor phenomena.

2. *Dysbasia Neurasthenica*.—This type is somewhat more difficult to diagnose particularly from intermittent claudication of the spinal cord.

Charcot cites an example of a lieutenant who could walk fairly well in the normal march, but at a faster pace would become unsteady after 20 to 30 minutes, his right limb particularly becoming heavy. With this there was marked numbness of the sole of the foot; all of the symptoms disappeared after rest. The patient, who was markedly neuropathic, was neither arteriosclerotic, leucic, nor diabetic. Objectively the pulses were negative and vasomotor phenomena absent. The knee reflexes were increased, and there was a right sided ankle clonus. Because of the marked neurasthenia, an affection of the spinal cord was believed to be absent. This diagnosis was confirmed 7 years later by Bourgeois, who observed that the same patient was still unable to carry on his activities.

3. *Sciatica*.—Here we must consider those relatively mild cases of sciatica in which paroxysmal attacks of pain are evoked only by motion, and call forth restriction of function. The pain in these patients does not abate as quickly as in intermittent claudication, and furthermore during the free intervals, pressure on Walleix's point should provoke the latent pain.

4. *Akinesia Algera*.—In this psychasthenic affection pain is aroused immediately upon the beginning of motion, and can occur not only in the extremities, but also in the back, in the head and elsewhere.

5. *Tarsalgia and Metatarsalgia*.—Here too pain follows short periods of locomotion and is localized to the tarsus and metatarsus. The arteries are intact and vasomotor phenomena are absent. There is usually a circumscribed area of tenderness.

6. *Certain Rare Cases of Neuritis*.—Cases have been described by Hallion and Charcot¹ as examples of neuritis, but the histories are not convincing, since the evidences of arterial involvement are sufficient to make it impossible to exclude these as a factor in the symptomatology.

CHAPTER XXVII

FORMS OF GANGRENE

One of the oldest classifications and one which has but little value since it throws no light upon the etiology, is the subdivision into *dry* and *moist gangrene*. Some authors add another variety, *microbic gangrene*.

¹ Hallion and J. B. Charcot, Arch. de Neurol., Feb. 28, 1895, XXIX, p. 81.

Dry gangrene ensues when the arterial circulation is suddenly impeded while the venous flow continues, the tissues being drained of their fluid through the veins. Mummification follows and the part becomes desiccated or dry by reason of loss of water. In man it is usually the peripheral parts that are affected. Perhaps mummification is a more descriptive word. This variety is not infrequently met with in the aged, when, by virtue of the slow process of athero- or arteriosclerosis, the lumina of the arteries become occluded, the blood supply diminishes progressively, and finally gangrene of a distal part occurs. Although the words *senile* and *dry gangrene* have at times been used synonymously, this restricted application of the term is incorrect, since dry gangrene takes place in many other conditions.

After preliminary blanching, paresthesiæ, coldness and loss of sensation, cyanosis usually follows. The skin gradually becomes dry, then brownish or black, the whole part being converted into a shriveled, hard, blackish mass. The changes in color are ascribed to the disintegration of hemoglobin with the elaboration of black by-products.

Moist Gangrene.—Moist gangrene results when there is an impediment both to the influx of arterial blood and to the venous return, so that the affected part retains sufficient fluid to leave the dead tissues moist. Complete obstruction of the chief veins of a part, without occlusion of the arteries, may also lead to gangrene, although this is of rare occurrence. The condition of the circulation in the limb before the arrest of arterial circulation takes place, may be the determining factor in the production of either the moist or dry type of gangrene. Intense edema associated with nephritis or impaired heart action usually favors the development of moist gangrene, as in the embolic or thrombotic gangrene, complicating pneumonia or other infections.

Because of the putrefactive condition characteristic of this process, *putrid gangrene* would be an apt designation. The sequence of events is first degeneration of the blood with the appearance of dirty red patches and zones. Then the connective tissue and muscles undergo change, whilst epithelium, tendons, elastic fibers, cartilage, and bone are most resistant.

The parts become doughy, edematous, the epidermis is separated off in blebs; there may be gas formation (NH_3 , SH_2 , or $\text{S} (\text{NH}_4)_2$), crepitation and foul odor. Leucin, tyrosin, triple phosphates, blackish pigment and fat crystals are to be found in the fluids. In addition to putrefactive organisms, streptococci often develop and may enter the blood stream. *Bacillus coli* may also be associated, and the *bacillus proteus vulgaris* may grow in symbiosis with either of the above and enhance their virulence.

The general clinical picture is an expression of the absorption of toxins (especially of proteus) with or without the effects of streptococcus or *bacillus coli* bacteriemia.

Characteristic for moist gangrene are the following clinical stages:—first, a stage of pallor which may pass so rapidly as to be overlooked; second, a stage of extensive ecchymosis; third, a stage of subepidermal exudation with reddish discoloration of the part; and fourth, a stage of disintegration.

Although these stages are not always clearly defined, they may be recognized in a fairly large percentage of the cases. The initial pallor may be evanescent; it may be accompanied with paresthesiæ but more regularly with frigidity and anesthesia. Soon a bluish and purplish mottling that rapidly spreads over the affected part becomes the striking objective manifestation, being succeeded by the exudation of bloody serum under the epidermis. When the latter is lifted off, larger or smaller bullae are formed

PLATE I



Early Stage of Moist Gangrene, Showing Bullæ. (Buerger in Ochsner's "Surgery,"
Vol. IV.)



Later Stage of Moist Gangrene. (Buerger in Ochsner's "Surgery," Vol. IV.)

PLATE III



Third Phase in the Appearance of Moist Gangrene. (Buerger in Ochsner's "Surgery,"
Vol. IV.)

(Plate I) many of which attain considerable size. When the epidermis has been separated and no considerable fluid is present, the angry red cutis vera shines through (Plate II). Higher up, the limb is usually cold for a variable distance, often intensely edematous and brawny, mottled here and there by areas of purplish discoloration (ecchymosis). Later the intense red disappears, as the disintegrating cutis vera and the gray green epidermis combine to form a peculiar ashen purplish hue (Plate III). The serum from the bullae now makes its escape in many places, the separated epidermis lying in folds over it, here and there torn off, exposing the weeping derma. With the advent of putrefaction, an intensely foul odor develops. Secondary pyogenic infection complicated by lymphangitis and cellulitis above the site of gangrene may supervene and be associated with toxic general symptoms.

Microbic gangrene has been termed acute microbic gangrene, fulminating gangrene, emphysematous gangrene and traumatic spreading gangrene. Here a virulent infection usually with a gas producing micro-organism is responsible for the mortifying process, injury usually preceding the infection.

If descriptions of this type be taken from older authors, a rather confused clinical picture will be obtained. Latterly, our notions have been considerably clarified since advances have been made in bacteriologic recognition of varying types. Special attention has been focussed on the gas-bacillus forms of infection, which will be discussed at length in another chapter. A number of different micro-organisms have been isolated and identified as the causative agents in this severe form of infectious and gangrenous process.

There is still another "infectious" or microbic type of gangrene in which gas formation is absent and in which the streptococcus can often be isolated in pure culture. A more comprehensive description of this variety will also be given elsewhere.

Course and Termination.—Gangrene is very frequently self-limiting, a definite line, separating the dead and the living tissue known as the *line of demarcation*, being ultimately formed. At this line granulation tissue is developed, as the result of a reactive inflammatory process. By virtue of the action of the emigrated leukocytes, certain ferments are elaborated which bring about the separation of the dead from the healthy tissue. Soft parts yield relatively soon to the sequestrating effects of the inflammatory process, whilst bone is very much resistant. When a considerable part of a member is thus separated off, so-called *spontaneous amputation* results.

When the area of necrosis or mortification is infected, the process of separation is accomplished in a different manner. The usual phenomena of suppurative inflammation of greater or lesser virulence are manifest, the products of inflammation being instrumental in causing disintegration of the part at its junction with the living, but may also spread in the healthy tissues requiring surgical intervention. If sufficiently severe, a rapidly ascending lymphangitis may occur, general infection, bacteriemia and toxemia. In these cases the end-result will depend upon the virulence of infection, and of the possibility of its control.

CHAPTER XXVIII

CLASSIFICATION OF GANGRENE

From the clinical standpoint, a pathological and etiological grouping is most satisfactory. It must be remembered, however, that an absolute classification is impossible, both because case may simultaneously belong to several groups, and because the causative factor in certain instances is not well understood.

Three large groups may be recognized: first, gangrene due to external or direct causes, such as bring about immediate death of tissue; second, gangrene due to internal or indirect causes, which act by impeding or arresting the circulation of blood in the larger vascular channels; and third, neuropathic gangrene in which the cause is an abnormal, pathological, functioning vasomotor nervous mechanism, or resides in the vegetative nerves.

A. External or Direct Causes.—(1) *Mechanical Causes* in which death or necrosis is the direct result of the physical injury. Tissues may become completely separated in continuity and thus die; or, necrose because of the disorganizing effect of a crushing force. Continuous pressure upon bony prominences, particularly in the emaciated, produces gangrene or necrosis to which the name *decubitus* has been given. Compression by a tight bandage, torsion acting upon a portion of the intestine, or strangulation at the neck of a hernial sac—all are mechanical causes of gangrene.

2. *Thermic Causes*, intense heat or cold, may cause death of tissue in a very short time, either by the direct coagulating or carbonizing effect, or indirectly by the formation of thrombi in the vessels, or by paralytic action on the vessels of supply.

3. *Chemical Causes* include the action of a fairly large number of substances. Some authors include some of the bacterial toxins, although many of these would not properly belong here, if their action were understood. The action of tissue juices in the normal secretions and excretions may, however be included here, since they produce digestion necrosis.

The most common chemical substances leading to gangrene are strong acids, hydrochloric, nitric, sulphuric, acetic, trichloracetic; also carbolic acid and lysol when applied as wet dressings. The secretions and excretions that bring about necrosis through their specific ferments are gastric juice escaping through a gastric fistula, extravasated urine, and the feces.

4. *Microbic Agents*, certain virulent bacteria, particularly in the presence of intense traumatism, may bring about a combination of infection and gangrene often called *microbic gangrene*.

The toxins produced in bacterial inflammation are also regarded as being responsible for destruction of tissue, or even for gangrene.

B. Internal or Indirect Causes.—*Injury of the main nutrient vessels* may be brought about by mechanical force in several ways, as when a limb is crushed or receives an intensive trauma, when a large vessel is pierced by a gun-shot, when pressure effects are produced by an aneurysm or a malignant tumor, then the circulation may be impaired indirectly, through interference with the continuity or patency of the chief nutrient vessels. Ligation of a vessel, such as the spermatic artery during an operation upon the testicle, or for hernia, or ligation of a renal or middle colic artery, may lead to necrosis and gangrene. Ligation of the internal carotid artery is followed by necroses of the

brain, in almost 50 per cent of the cases. In the case of the extremities, ligation of one of the main arteries may be followed by gangrene if adequate collateral circulation does not become established. The general condition of the patient, the heart action, the presence of complicating diseases (such as anemia, diabetes, infections and atherosclerosis), of inflammatory conditions, exudates or hematmata in the affected limb, and tight bandages—are all contributory causes that hinder the establishment of collateral circulation.

Diseases of the blood vessels including first athero- or arteriosclerosis (senile, presenile, diabetic, with or without thrombosis and embolism); second thrombo-angiitis obliterans; and, third, endarteritis (including syphilitic endarteritis); and fourth, acute arteritis and miscellaneous affections.

Thrombosis or Embolism.—Complete obliteration of the lumina of either normal or diseased vessels through thrombi or emboli may lead to gangrene. When these occur in diseased vessels, they may be regarded as complications of the primary vascular lesion. Therefore only such obturation in vessels relatively patent will be discussed under this caption.

Emboli and thrombi may be composed of red clot, mixed clot, bacteria, purulent or even tumor material. For practical purposes we need consider merely clots; other embolic material more frequently evokes small areas of necrosis, suppuration or aneurysm, than true gangrene.

Embolism most frequently affects the femoral or popliteal artery and may then result in gangrene of the foot and leg. More rarely the brachial and axillary arteries are involved. It occurs most commonly in the course of severe infectious diseases, or as a complication after the disease has subsided, also with valvular heart lesions, and after abdominal or pelvic (particularly gynecological) operations. In typhoid fever, pneumonia and influenza, sudden blockage of the popliteal or femoral artery may occur, or there may be extensive thrombosis of the femoral vein. Although it is not generally understood why an embolus in the popliteal artery should cause extensive gangrene, when there are adequate avenues of blood supply through collaterals, the explanation is often to be found in the fact that extensive red thrombosis is soon superadded above and below the site of the original clot, red and mixed thrombi extending in both directions with great rapidity into many of the smaller vascular branches and tributaries, preventing in this way the establishment of a subsidiary collateral circulation.

C. Neuropathic Gangrene.—In this group may be placed all those cases in which the arteries and veins are organically intact, or have suffered no alteration of their patency, and in which, in the present state of our knowledge, we assume that a neurogenic causal agency is responsible.

The following symptom-complexes, Raynaud's disease, erythromelalgia, acroparesthesia, multiple neurotic gangrene, and chronic acro-asphyxia belong here. It has been generally accepted that in some of these, the vascular disturbances and arrest of circulation may be accounted for on the theory of a spastic condition of the nutrient vessels, but in others, the true mechanism still remains unrecognized.

The various clinical forms of gangrene will be grouped and described according to the following classification:

I. Gangrene due to external or direct causes, viz.:

- A. *Trauma.*
- B. *Thermal influences.*
- C. *Chemical causes.*
- D. *Microbic action.*

II. Gangrene due to indirect or internal causes, including

A. *Injury to main nutrient vessel of a part.*B. *Diseases of blood vessels.*1. *Arteriosclerosis.*2. *Thrombo-angiitis obliterans.*3. *Endarteritis (luetic).*4. *Miscellaneous arterial affections.*C. *Thrombosis and embolism.*

III. Neuropathic gangrene.

CHAPTER XXIX

CLINICAL EXAMINATION IN GANGRENE

Examination in Prodromal Stages.—In order to understand and give the proper dignity to all of those clinical manifestations that constitute the prodromal signs of symptom-complexes that eventuate in gangrene, it is wise to follow a certain scheme of procedure in the examination of all cases in which we suspect impaired circulation. When we are confronted with cases of vasomotor disturbance, of trophic disorder, such as ulcers and atrophy, when the patient complains of pain which arouses the suspicion of intermittent claudication, as well as in the presence of true gangrene of the lower extremities, the following method of the author will be found of value in diagnosis. It includes the investigation of the following points: First, the general appearance of the limb in the horizontal position; second, in the dependent position; third, the presence or absence of ischemia in the elevated position; fourth, the estimation of the *angle of circulatory sufficiency*; fifth, pulsation in the palpable vessels, iliac, femoral, popliteal, posterior tibial, anterior tibial and dorsalis pedis in the case of the lower extremities, radial, ulnar, brachial and axillary in the upper extremities; and, sixth, the occurrence of *induced, reactionary rubor* or *erythromelia*. The value of nerve status need hardly be emphasized.

1. *General Appearance of the Limb.*—Any departure from the normal should be noticed, such as the presence of fissures, ulcers, perforating ulcers, bullae, ecchymoses, impaired nail growth, gangrenous areas, distinct gangrene, signs of infection or lymphangitis or venous thrombosis. Evidences of malnutrition, such as atrophy, exceptional prominence of the bony landmarks and extensor tendons, conservation or effacement of the normal irregularities of contour through edema or through thickening of the skin and subcutaneous tissues, are features of importance. Variations from the normal color—particularly marked pallor in the horizontal position, a play of color over the foot, even in the horizontal position; cyanosis, increased redness—all these, are manifestations of either impaired circulation or vasomotor disturbance.

2. *Rubor or Erythromelia.*—With the foot in the pendent position and in the absence of inflammation, a red flush involving the toes and dorsum, as well as sole of the foot, extending upward for a variable distance, rarely farther than the ankle, is a phenomenon that is characteristic of many cases and many types of reduced circulation due to vascular obturation. This is a

condition of *rubor* or *erythromelia*¹ (Gr. *erythros*-red, *melia*-limb). It is brought about by a compensatory dilatation of the superficial capillaries, and is most characteristic of the disease, thrombo-angiitis obliterans, although also found in other arterial affections attended with closure of larger vessels. It is frequently present in arteriosclerotic and diabetic cases as well. It seems to be an effort on the part of nature to make up for the impairment of circulation by virtue of dilatation and engorgement of the superficial capillaries. Although more striking in the pendent position, the rubor may also be present in the horizontal position, and when continuously in evidence, may be termed *chronic rubor*, *chronic erythromelia*, in contra-distinction to the *reactionary rubor* that may be induced by depressing the limb after previous elevation. These terms, *erythromelia*, *chronic rubor*, *reactionary rubor*, *induced rubor*, *angle of circulatory sufficiency*, as well as others employed here, have been adopted by the author in an attempt to facilitate expression of various conditions of circulation, and if adopted, must be carefully applied in the sense here suggested.

3. *Ischemia or Blanching*.—This usually sets in rapidly when the affected limb is elevated, whenever mechanical interference with the circulation is present. The extent of the blanching and the rapidity with which it appears, are both valuable aids in the estimation of the amount of obstructive arterial disease. When the affected limb is cold, the tips of the toes may remain slightly blue or cyanotic. Should the blanching be slow in appearing, or very hard to determine, pressure upon the tips of the toes after the limb has been elevated for some time will demonstrate whether the part has become depleted of blood or not. Before elevation, pressure over the toes will cause an anemic area in which the color returns tardily (Expression test). Compression of the toes of the elevated foot in normal cases will reveal the presence of sufficient bright arterial blood (rarely slightly cyanotic), whilst a varying degree of ischemia, with or without marked cyanosis will accompany obliterated or obstructed arteries.

4. *The Angle of Circulatory Sufficiency* (Fig. 43).—The estimation of this angle is based on the supposition that the normal limb, when elevated so as to be perpendicular to the horizontal plane, that is 180° , still retains most of its color. When the circulatory mechanism is defective, and the limb is elevated to the vertical, a variable degree of blanching of the foot occurs. If the leg is then gradually depressed, *the angle at which a reddish hue returns* (angle of circulatory sufficiency) will be found to vary considerably. In some cases it will be necessary to depress the limb to the horizontal before evidences of return circulation are manifest. The angle of circulatory sufficiency would then be 90° . If the reestablishment of visible circulation in the skin necessitates depression below the horizontal, the angle will be correspondingly less than 90° . In many cases of arterial disease, the estimation of this angle is a valuable adjuvant, not only in the recognition of the extent of the circulatory disturbance, but also in prognosis.

When the deficiency in color of the foot appears but slight or doubtful, it is well to examine the sole of the foot flexed at right angles with the patient in the prone position. The difference in the color of the two feet may thus become more apparent. When infection is present, tenderness over the plantar region will often be elicited, and indicate deep necrosis or suppuration complicating a gangrenous digit, even though no superficial sign thereof—such as redness—be in evidence.

¹ Not to be confused with "Erythromelia" a term used by Pick to designate an atrophic cutaneous malady.

Vasomotor symptoms may interfere with the estimation of the angle of circulatory sufficiency. Sometimes the blanching of the foot together with the cyanosis induced after elevation may remain so long, that the angle cannot be determined. In these cases it is not the obstruction of the vessels, but the special vasomotor irritability that is responsible for the lack of usual reactive hyperemic response; for, neither is it constant, nor does it regularly interfere with the test. Such vasoconstriction is also not always present to the same degree. It is, therefore, incumbent upon us to apply the test on several occasions, to preclude the fallacies that vasomotor lability may occasion.

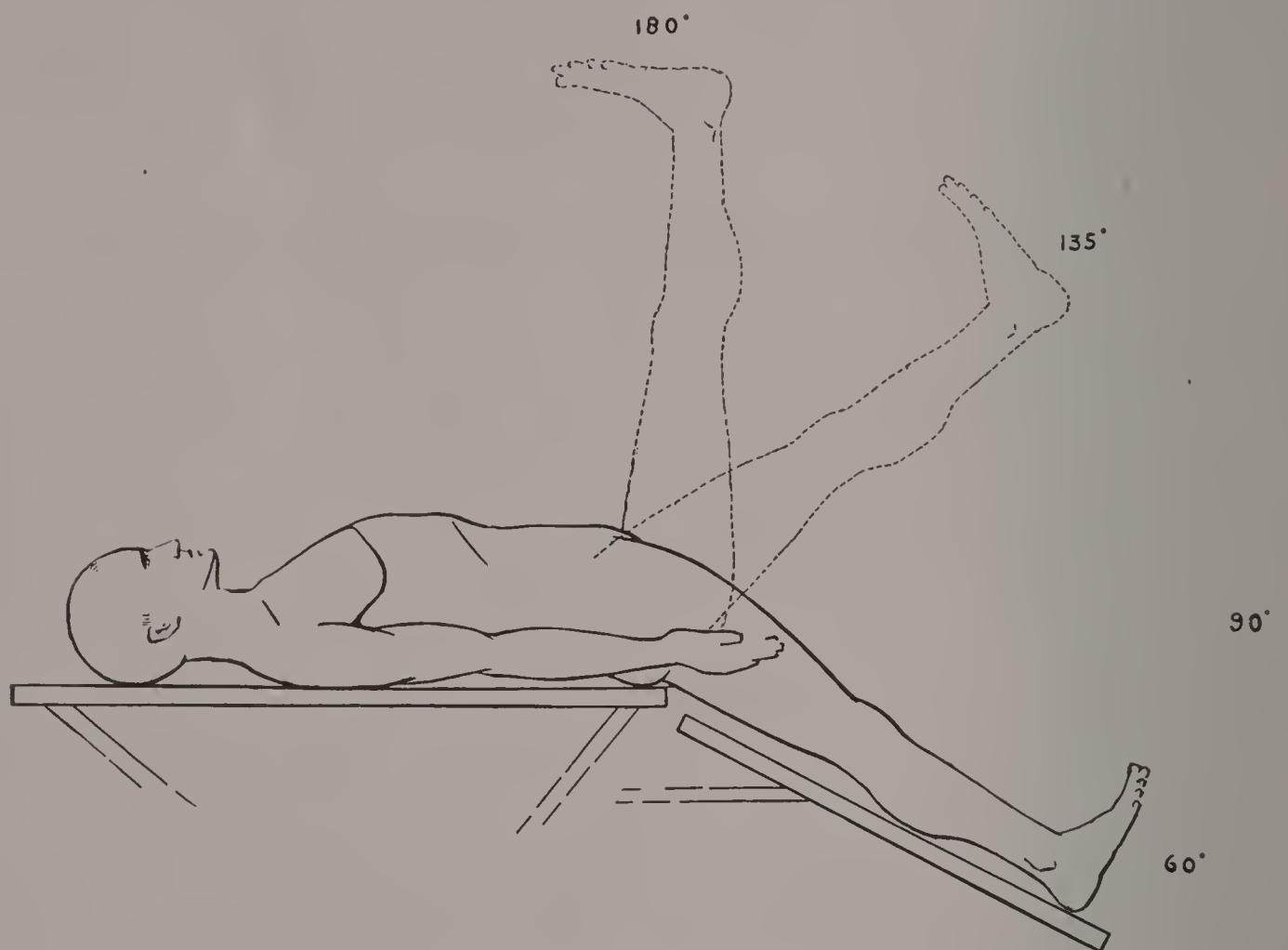


FIG. 43.—Method of determining the angle of circulatory sufficiency.

By a comparison of the circulation of both lower limbs, valuable information can be gleaned as to the degree of involvement of the arteries in each, also in the corroboration of a presumptive diagnosis of obliterated arteries in the limb that gives no subjective symptoms.

So it may be necessary to depress one limb from 180 to 90° (horizontal) in order to effect a return of color into the toes, whilst in the other, a complete blush occurs at 135° (45° more elevated). The circulation may show visible advance up to a certain point (such as the base of the toes) at one angle, and still greater pendency may be required to promote a flux into the toes. These or even more of the foot may remain cadaveric in hue until the horizontal or possibly a lower position is reached.

5. *Absence of Pulsation as an Indication of Arterial Occlusion.*—We should be able to feel the femoral, posterior tibial, popliteal, and dorsalis pedis arteries, pulsating in almost all individuals who possess patent arteries. In rare cases the dorsalis pedis may be aberrant in its course, and there-

fore not palpable in its usual situation, or, neither the dorsalis pedis nor popliteal may be accessible to the touch because of the stoutness of the patient.

To palpate the popliteal satisfactorily, the patient is placed on his abdomen, lying prone. The leg is held at right angle, that is, vertical, the patient being asked to relax the hamstring muscles. The artery is then sought in the upper half of the popliteal space, just outside of the semimembranosus and semitendinosus tendons (Fig. 42), the fingers being pressed downward against the femur. In the upper extremities, the radial, ulnar and brachial and axillary arteries should be examined for pulsation.¹

The absence of pulsation is as a rule, an indication of occlusion at the point palpated, *although in some instances dissections have shown that the site of obliteration is somewhat higher up.*

6. *Reactionary Hyperemia, Rubor or Reactionary Erythromelia.*—By this term we mean an *induced rubor* that manifests itself in the dependent position of the foot, after it has been previously elevated to the vertical. It is a physiological phenomenon, that ischemia or blanching of a limb artificially produced by an Esmarch or Martin bandage, will be followed by sudden dilatation of the capillaries of the peripheral parts, when the circulation is allowed to return. *So, also blanching will occur in a leg whose larger arteries are occluded, on mere elevation from 60 to 90° above the horizontal, without the use of any artificial means.* When such a blanched limb is then depressed to the pendent position, a similar induced or reactionary rubor will become manifest. This well-known manifestation may be invoked in the examination of cases in which impaired circulation due to arterial occlusion is suspected. It will be found particularly useful in cases of thrombo-angiitis obliterans, although also demonstrable in other cases of organic vascular disease. In early cases, it is a particularly valuable sign, for it may be present long before the chronic condition of rubor or erythromelia develops.

It is a manifestation analogous to the hyperemia (Bier) induced by the application of an Esmarch or similar bandage or tourniquet to a limb, immediately after the arterial compression is removed.

In a sense all chronic *rubor* of the pendent position is a *reactionary rubor*, when it accompanies obstructive arterial disease. For, is there not always a relative ischemia of the peripheral parts; and is not this brought about in varying degrees by every elevation of the limb, even if only to the horizontal? Indeed, it will be elsewhere shown (page 238) that in cases of marked impairment of the peripheral circulation, the foot is already blanched in the horizontal position, or even when flexed slightly below this level.

Tests for Circulation.—It is indeed desirable to possess a sign, criterion or symptom that would afford a measure of the circulatory intensity of the leg, above the usually gangrenous parts of the foot. Search has been made for single phenomena that might fulfill this desideratum and a number of tests have been evolved. Among these may be mentioned those of Moskowicz, Matas and the author.

We shall refer later to the limitations of such evaluations and to the importance of that incommensurable and inestimable factor—the excessive demands for healing. For, when investigations of the degree of force and extent of collateral circulations are practically applied, they have been regarded by many authors as especially valuable in determining the lower safe limit for amputation. In our own experience, all such tests are more reliable in fore-telling

¹ Some of the anomalies of the radial and ulnar arteries are mentioned in Chap. II.

the probabilities of the healing of the trophic disorders, or in fore-casting the advent of gangrene, than in setting indications for the site of operation.

*The Moskowicz Test.*¹—This depends on the phenomenon that soon after removing an elastic bandage that has set the circulation of a limb in abeyance, an active hyperemia replaces the cadaveric hue. This striking rubor begins at and is sharply demarcated above, at the level of the constrictor. Thence it extends rapidly, down the extremity (peripherally) till it reaches the tips of the toes or fingers.

After holding the extremity high for a short time (and this concerns especially the lower) an elastic bandage is firmly applied as far up as possible and allowed to remain for 5 minutes. After removal of the constrictor, a prompt hyperemic blush is to be expected, when the circulation is adequate. When vascular obturation exists, the reaction is weaker and the extension of the blush towards the distal parts is slow. Often ischemic islands in the skin seem to tarry for some time, and in some instances a marmorated appearance will be prolonged. The hyperemia may progress rapidly to a certain level where its further spread is arrested or allowed to descend very slowly. In comparison with the less affected normal limb, the persistence of peripheral pallor in the more diseased extremity will be found most striking.

Moskowicz is of the opinion that the lower boundary of the hyperemic zone or point just above this, marks also the level of the obturation of the arteries. Reasoning thus, he sets the indications for the proper niveau for operation by selecting a level within the area of reactionary rubor—namely a short distance above its peripheral limitations.

In our own experience this test is unreliable. Indeed, certain dogmatic and arbitrary rules that we have adopted as the result of a multitude of clinical observations are to be followed, in the selection of the level for amputation, rather than teachings such as the above.

*The Matas Test.*²—This is a modification of the Moskowicz test for estimating circulatory sufficiency in cases of aneurysm. Although the purpose and technic of the Matas method are somewhat different from that of the latter, they are similar in utilizing the hyperemic blush following artificial ischemia to determine the limits of adequate circulation. The principle according to which this test is employed is based on the fact that whilst the main arterial trunk is compressed in close proximity to the lesion (wound, aneurysm, tumor) sufficiently to arrest pedal pulses or fill an aneurysm, the collateral distribution is allowed to give evidence of its extent and magnitude.

This segregation of the visible signs of collateral from those of the normal circulation is obtainable by excluding the main artery as a factor through compression, simultaneously with the abolishment of all impediments to arterial flow through other channels.

An elastic bandage, after preliminary elevation, is applied from the digits to the level of the lesion, usually the aneurysm, after which a compressor is applied to the artery above the aneurysm. The elastic bandage remains in situ for 10 minutes in the young, 5 to 6 minutes in the aged, and is then removed, whilst the main artery is completely occluded. Immediately upon removal of the bandage, a hyperemic blush descends downward rapidly, progresses onward to variable extent, *in proportion to the development of the collateral circulation*. More often, the hyperemia may stop at a distance of 5 or 6 inches from the compressor, or about $\frac{1}{4}$ distance down the limb, then

¹ Moskowicz, L., Mitt. d. Grenzgeb. d. Med. u. Chir., Vol. XVII, p. 216.

² Matas, Jour. Am. Med. Assn., 1914, p. 1441.

continuing in a subdued color, traveling towards the periphery, but the extreme end of the limb, foot, or hand retains a cadaveric waxy pallor for several seconds or even 40 minutes, according to the development of collaterals. Then this waxy color gives way to a pale living color. Where collaterals are well developed, the hyperemic wave spreads in a few seconds, as if the artery had never been compressed.

Matas in 1914 had used this test in 26 cases of aneurysm and other lesions, and the conclusions furnished by this test have been invariably confirmed by operative demonstrations and results. He used this test therapeutically in several cases, where the reaction was long delayed, for the purpose of increasing the collateral circulation, as follows. He postponed operations for days or weeks, in order to develop collateral circulation by systematic compression of the main arteries, conjointly with dry hot air, baths and massage.

Whilst the Matas and Moskowicz tests may have a sphere of applicability when a limited arterial territory suffers obturation, they are not very reliable in peripheral vascular disease. In thrombo-angiitis obliterans or marked arteriosclerotic disease of the vessels, certain elements of these tests would need modification. The application of an Esmarch bandage is not to be recommended in view of the deleterious effects of such intensive ischemia, and the direct mechanical lesions that might ensue. Furthermore, the peripheral pulses are not usually palpable, and therefore no guidance. It has been the author's custom to employ a method based on hydrostatic principles which has been previously described. In view of the extensive vascular obliteration that accompanies thrombo-angiitis obliterans, it is noteworthy that no great differences can be elicited at times, between the color reaction that follows the depression of the limb after prolonged elevation (gravity depletion), and that resulting after separate compression of a main artery. This is comprehensible when we consider that the very main vessel compressed may have become a negligible factor in the delivery of blood even through collaterals; and when we take into consideration the multitude of occluded branches emanating from this trunk. In other words, such main arteries are not essential to complete the collateral circuit and the latter depends on even more remote and deeper channels and anastomoses.

Allan and Matas have also experimented with the occlusion of the main artery by flat and pliable aluminum bands. Such a band is applied about the vessel supplying the part to be tested. If the collateral circulation is adequate, the band is left in place, and becomes encysted in the tissues. If gangrene threatens, the band is made more lax, so as to facilitate a better collateral circulation. The bands are made long and narrow so as to pass through aneurysm needles. After such a band encircles the vessel, it is tightened with the fingers until the pulse is obliterated distal to it.

Value of Tests for Circulation in Thrombo-angiitis Obliterans.—The Moskowicz test according to some authors is of value in determining the safe point to amputate in presenile and in senile gangrene. Matas cites examples in which he was successful in recognizing that amputation could be performed below the knee, because the hyperemic blush extended well below this level, thus indicating that a flap would be viable.

The author's experience in cases of thrombo-angiitis obliterans has convinced him that, although the test may demonstrate to what extent a collateral circulation has become established or even how far a compensatory hyperemic state has been developed, it does not, with any degree of precision or reliability, denote where amputation should be carried out. This is true because it cannot correctly gauge the likelihood of healing after an incision is made, even though it demonstrates the centrifugal limit of collateral skin circulation. For, it must be remembered, that not only is it necessary to

have blood enter the most peripheral parts after amputation, but nature makes excessive demands for purposes of healing. The exigencies evoked by the new conditions may be incommensurate with, and far exceed those hydrostatic factors that are sufficient to give a red color to the part. Not infrequently has gangrene of the flaps and other tissues at the point of ablation been observed when the Moskowicz test indicated ample collateral paths. Even when healing of the greater part of the wound does occur, an ulcer may remain at the point of drainage. This is then wont to enlarge and gives rise to gangrene or phlegmon formation.

In short, experience in thrombo-angiitis teaches that an indication for amputation below the knee or below the level of the Gritti-Stokes method, set according to tests, is of theoretical rather than of practical value. In arteriosclerosis amputation below the knee is also unreliable, although in rare cases it may be attended with good results.

Henle-Coenen Method.—Almost simultaneously Henle, Lexer, v. Frisch and Coenen recorded an observation which they regard of value in estimating the degree of collateral circulation. It was applied by these authors to the treatment of aneurysms by ligation. In their judgment, indication for ligation would depend upon the positive result of the test. If a larger artery be sectioned transversely, not only the central but the peripheral stump should bleed copiously in a strong stream (Positive test).

It is based on the fact that in many arterial territories (external carotid, arteries of the hand and foot), the normal collateral circulation suffices to give a copious reflux when the centrifugal current is interrupted at any point.

Tests for the Patency of the Veins.—Whereas it is a relatively easy matter to determine with a fair degree of certainty whether the patient possesses patent superficial veins, the question as to the involvement of the deep veins is a most puzzling one. Thrombotic lesions in the palpable veins are described in detail in Chap. LVIII. In these latter cases one can watch the recurrences of thrombophlebitis throughout the thigh and leg and find it extending even to the sole of the foot. And, when personal observations are not at hand, anamnestic data may be forthcoming.

What signs and symptoms are of value in indicating the patency or occlusion of the deep veins? It is here that we have to concede the inadequacy of our clinical methods. In looking over the histories of the cases in which amputation revealed marked obliteration of the deep veins, only in very few was there mention of marked cyanosis in the pendent position of the limb. Whilst an unusual intensity and rapid advent of cyanosis after rubor may be a serviceable sign in this connection, it is not absolutely dependable since vasomotor agencies play an important rôle in the determination of color phenomena. Inadequate vis à tergo and constricted arterioles in a pendent limb may suffice to give cyanosis without obstructive lesions of the veins.

CHAPTER XXX

TRAUMATIC GANGRENE

Traumatic gangrene results from the direct action of a mechanical force. A rapid and direct disorganization of tissue may follow mechanical insults such as contusion, crushing, machine injury, injury through blunt force, and

pressure. The latter force acts in the main by interference with circulation. Tissue which has become totally separated must needs become necrotic or gangrenous, if the conditions for healing and restitution of the circulation in the wound are not favorable. Such adverse conditions arise when severe traumata bring about crushing and mangling of tissue, extravasations of blood and bacterial infection. Only in the case of transplantation by operation under strictest aseptic conditions, are the conditions favorable for restitution and growth of the transplant.

A blunt crushing force may also lead to gangrene of tissue, partly by reason of the disintegrating and destructive action of the force itself, and partly through thrombosis in larger vessels. The severe traumata inflicted in various accidents by machinery, which produce extensive laceration of tissues, may be followed by gangrene of a part or the whole of an extremity.

We may distinguish a number of varieties. Through separation of continuity a mass of tissue may be detached and become necrotic, its attachment and healing being prevented by hemorrhage and infection, or through displacement of tissue elements (*Décollement*) and distortion, a blunt force leading to the formation of a subcutaneous pocket. Blood then fills this space; thrombosis of the torn and squeezed vessels takes place, and gangrene and necrosis are expedited. Or, ligations of vessels may lead to a similar issue, whenever the chances for the establishment of collateral circulation are slight.

Observations on the results of traumata during the Great War have awakened interest in the indirect effects of trauma. Through the stimulation of the vessel nerves, contraction and later dilatation of the smaller blood vessels occurs. Intense trauma may evoke dilatation and finally complete vascular paresis with stasis and diapedesis. An ischemic necrosis of muscle is described as due rather to the implication of nerves, spastic contraction of vessels, dilatation and stasis, than as the result of direct forces.

Finally, injuries leading to rupture and consequent ligation of larger vessels are not infrequently complicated by gangrene. Such an eventuality may be expected, when extensive hemorrhagic extravasations are present.

Symptoms. Manifestations of threatened gangrene of an extremity begin with the picture of ischemia or venous stasis, coldness, and absence of pulsations in the usually palpable arteries. After initial paresthesiæ, or dull pain, complete absence of sensation and motor paralysis set in. Intense pain and tenderness, however, may persist above the area of gangrene. Within forty-eight hours, the evidences of beginning dry or moist gangrene make their appearance.

It would be possible, although not fruitful, to make groupings according to the nature of the injury, its extent, whether the main arteries of a limb are implicated, as to whether the issue be gangrene of part or whole of a member, or merely limited necroses.

The following classification although not all-embracing has some clinical value.

1. Gangrene of limited extent involving larger or smaller areas of the integument, possibly attended with injuries (fractures or dislocations) of deeper parts.

2. Gangrene of part of an extremity, usually the lower, due to direct compressing forces with or without complicating thrombosis of the main artery; and

3. Gangrene of almost the whole of an extremity (usually the lower). The most striking and characteristic examples of this variety are those

severe injuries resulting from accidental entombment, so frequently observed during the Great War.

1. **Gangrene of limited extent** requires no detailed description. Whenever a limb is subjected to such compressive or percussive force that the vitality of the tissues is compromised, local necrosis ensues. When such devitalization with subsequent sequestration of slough is of limited extent, we usually speak of a "decubitus." This may occur after the application of too tight bandages, or after even slighter insults in those in whom neurotrophic and functional derangements already exist. More severe injuries, such as compressing, sliding and crushing forces against the extremities may result in more extensive death of tissue. These are seen in automobile, railroad and "shoot-the-chutes" accidents, where the living force and momentum cause an extraordinary degree of local stress when resistance is encountered. Even gangrene of a part or the whole of a limb may eventuate, especially if the main artery be traumatized and thrombosed.

2. **Gangrene of an Extremity.**—Traumatic gangrene of the lower extremity is best exemplified by that resulting from accidental entombment. The cases may be grouped into:

A. Gangrene with, and

B. Gangrene without blockage of the main arteries.

3. **Accidental entombment**, formerly of rare occurrence and rarely seen except in mining and building operations or earthquake, was not infrequently the cause of extensive gangrene of the extremities during the Great War. The injury to the extremities following such trauma is attributable to external pressure and is characterized by the absence of external wounds, the absence of severe external contusion, and of infection.

Similar injuries have been described as occurring during earthquakes and Colmers¹ reports acute decubitus as the result of such injury. The contusing force acts for many minutes or hours by reason of the fact that the injured person is imprisoned and incarcerated under earth, stone, debris, etc. Gangrene of a portion or the whole of the extremity, resulting from such a trauma is characterized by the absence of external wounds and of infection.

Acute traumatic decubitus is a condition resulting from incarceration of the body or entombment for many hours, the compressing forces bringing about localized gangrene. The skin, the soft parts, as well as the bones may become involved. Strange to say the integument may remain intact, whilst the fascia and muscles become necrotic. Subsequently infection leads to extensive phlegmon formation. The gluteal and trochanteric regions are the sites of predilection. After sequestration of the dead tissue, large punched out holes or cavities are left behind (Colmers).

A. **Gangrene with Arterial Thrombosis.**—The trauma is usually exerted over the thigh. The symptoms include rapid development of necrosis of the lower extremity without the presence of any wound or an infectious process. The lower extremity becomes enormously swollen, tense and indurated; the skin of the whole leg is discolored, has a livid hue, is marmorated with areas of pallor, sometimes with superficial excoriations. The whole limb is immobile and cold up to the knee or even higher. The pulses in the dorsalis pedis and popliteal are usually absent.

If the patient is not already in shock, the usual symptoms of the latter develop, and exitus occurs in most of the cases within a few days after the injury.

¹ Colmers, Arch. f. klin. Chir., 1909, 90, p. 703.

The femoral artery at the site of the greatest compression may be thrombosed, the intima injured and detached, or the seat of suggillations. Secondary thrombosis in the femoral vein develops later, and may contribute to the development of gangrene.

B. Gangrene Without Involvement of the Main Arteries.—Here we may distinguish gangrene of the leg with mortification of (1) the superficial tissues, or (2) the deep tissues.

1. *Traumatic Superficial Gangrene with the Main Vessels Intact.*—This variety is characterized by the fact that but a short time after release from entombment the picture of impending gangrene rapidly develops. The leg may be markedly swollen, cold and tense, the peripheral pulses absent. Changes in the appearance of the skin are striking in that the color is first bluish red and marmorated in places. Soon there develop large vesicles or bullæ partly filled with light colored fluid or blood. Signs of infection are usually absent. Shock is associated only in the cases sustaining severe trauma, but local pain may be severe. With the progress of the gangrenous process, temperature is common and amputation becomes indicated.

The cause of the tissue death seems to be the force of external pressure. Whilst complete mortification may involve all of the tissue lying upon the deep fascia, the underlying parts are the seat of hemorrhagic infarction and thrombosis of the smaller vessels. In spite of the fact that the vitality of the deeper tissues is not altogether compromised, their integrity and future outlook gives little promise of functional restoration. In spite, therefore, of only superficial necrosis, amputation usually becomes necessary.

Pathology.—The skin of the leg is usually extensively infiltrated with blood and the veins thrombosed. The subcutaneous tissues, too, show brownish black discoloration with numerous thrombosed vessels. As for the tissue under the fascia, the muscles may show but slight changes save for some hemorrhages. Except for some bloody extravasation, possibly bony fractures, all of the deeper tissues may escape the destructive mortifying process.

2. *Traumatic Gangrene of the Deep Tissues* (with main arteries intact).—Although the limb will here also give early evidences of interference with its nutrition, gangrene develops more slowly. Indeed, months may elapse before amputation seems warranted. The circulation of the skin may appear unimpaired for some time (Orth¹); or coldness and pallor may be present (Kuttner²) from the beginning.

The characteristic feature of this variety of traumatic necrosis is the disturbed nutrition of the musculature and the intensive swelling of the deeper tissues, the skin and subcutaneous tissue suffering relatively little. The latter may, however, become secondarily involved. Gangrene of the extremity does not necessarily follow especially if no secondary infection supervenes. Or the muscle alterations may subside if not too severe. In these circumstances function may become restored, or more or less permanently impaired.

In short, primary necrosis of muscles is believed to occur in these cases. Prolonged action of an equally distributed contusing, compressing force may explain the involvement of muscle and escape of the integument, in contradistinction to the more intensive stresses that bring about mortification of the skin.

¹ Orth, München. med. Wchnschr., 1916, No. 39, Feldärz. Beilage, No. 39, p. 1407

² Kuttner, Bruns' Beitr., 112, 1918, p. 591.

Treatment.—The treatment of traumatic gangrene includes first, the surgical treatment of the wound produced by the injury, according to the principles of aseptic surgery; second, the methods for enhancing the circulation, so as to limit the gangrenous process, as much as possible; and third, the amputation of the affected part. These methods will be given due consideration in Chap. LXV.

CHAPTER XXXI

THERMIC GANGRENE

Intense heat or cold may bring about necrosis of tissues within a very short time, while a moderate degree of heat and cold may have the same effect when in action for longer periods. Gangrene from cold apparently differs in no essentials from other forms of mortification. The death of tissue may occur first, from the direct action of cold upon the protoplasm; second, from the ischemia due to vascular spasm; and third, thrombosis. Although gangrene may be due to the fact that the part has become completely frozen, restitution would occur in most instances were it not for the fact that extensive thrombosis of the arterial and venous channels has already occurred.

For a thorough understanding of the gangrenous processes depending upon the action of cold, it is well to have some knowledge of the observations that have been made on the effects of such influences during exposure in time of war. It was during the recent Great War that a multitude of lesions dependent upon exposure to cold and moisture developed, many of which were accompanied by gangrene.

General Consideration.—In studying the effect of cold on human tissues we must take into consideration both the local and the general action. The human organism can adopt itself to very marked diminution in the surrounding temperature, without any considerable loss of body temperature. The body compensates for loss of warmth by increased heat production. So important is the matter of tissue nutrition that in the absence of an adequate delivery of blood the body warmth may be reduced to a degree incompatible with a continuance of the vital functions. The consequences of the local action of cold on the tissues vary according to the degree of temperature, the duration of the action, and the character of the environmental circumstances.

Cold, dry air has an effect different from cold water or snow, whilst the effect of air in motion is notably at variance from that of an absolutely tranquil atmosphere. These variations are due in part to the fact that loss of body warmth to the air is effected through radiation, whilst the physical process is one of conduction in a watery, humid, or moist medium. The red blood cells are said to be destroyed through freezing. Lesser degrees of cold produce primarily a constriction of the vessels, first of the smaller then of the larger arteries. The pain due to cold results from the direct action of loss of warmth upon the sensitive nerve endings. Consequent upon vasoconstriction comes vasodilatation, when the temperature rises; and redness and cyanosis of the exposed part ensue.

A wet cold is especially apt to bring about marked redness and swelling of the part, in anemic individuals. Such individuals easily develop chilblains (pernio). The protracted action of moderate degrees of cold (not approaching the freezing point) may so disturb the arterial circulation, as to produce ischemia of the peripheral parts—toes and fingers—and gangrene. This ischemic type of gangrene must be distinguished from the immediate and actual result of freezing of a part.

Experimental work on the local lesions due to cold has produced a number of interesting lesions, among which may be noted the following; thromboses of the vessels (Hodara and Riehl); dehydration and ice formation in the tissues (Rischtler).

Symptomatology of Local Freezing.—Freezing of the tissues may be divided into three types. First, simple freezing with erythema as the chief symptom (first degree chilblain); second, with formation of vesicles; third, with gangrene. A fourth type has been suggested by Flörcken,¹ without skin lesions.

It was found during the Great War, that robust and strong individuals, who had been exposed for a considerable period of time in wet trenches, or had worked in cold water, presented the following clinical picture. There was severe pain, stiffness in the legs and back, with inability to use the muscles. Muscles, tendons, periosteum and the shin bone, as well as nerves seemed to be tender to the touch without any palpatory lesions, without objective changes of sensibility or altered reflexes. The most frequent localization of these symptoms was the region of the shin bone. Certain German authors have given the name “Schienbein Schmerz” to this syndrome.

The result of exposure during the war sometimes gave clinical pictures simulating influenza, typhus, perityphus and other diseases. Thus, Sippmann described headache, chills, fever, malaise as preceding the attacks of pain. The relationship between the characteristic tibial pain, and the general symptoms has been a mooted question. There can be no doubt, however, but that the intense pain in the extremity can be brought in direct causal relationship with the exposure to cold.

Local Changes Due to Cold. *First Degree.*—Portions of the body exposed to cold become reddened, whilst severe burning and prickling sensations are experienced (nerve irritation). As a result of vasoconstriction the parts become blanched and anesthetic. Rubbing of the parts may restore circulation. Following the vasoconstriction, intense reddening of the peripheral parts with itching and pricking sensation follows, the extremities becoming swollen. All of these symptoms may subside completely or lead to the development of chilblain. These are represented by bluish red, flat swellings, or nodular elevations surrounded by a red zone. The sites of predilection are the extensor aspects of the fingers and toes, the margin of the foot, the heel, the ball of the foot and the back of the hand. However, ears, nose, cheeks, and more rarely the penis, the gluteal region, and the chin may be affected.

Second Degree.—Freezing of the second degree is characterized by the presence of bullae or vesicles on a reddened or violaceous skin. The contents of the vesicles differ from those of gangrenous vesicles in that there is clear fluid just as in the blebs of burns. After the bursting of the vesicles the superficial epithelial defects heal rapidly. In rare cases, however, ulcers may form that are of indolent character. Certain authors have brought these lesions into relationship with subsequent arterial changes eventuating in gan-

¹ Flörcken, *Ergebn. d. Chir. u. Orth.*, 1920, p. 185.

grene (Von Winiwater). The particular disease, however, described by this and other investigators has been shown by the author to be none other than thrombo-angiitis obliterans.

Third Degree.—When the fingers or toes suddenly turn blackish and cannot be moved, lose their sensation and become cold as ice, we have the typical picture of this form. When the superficial portions have been damaged, then needle pricks and incisions are not experienced as pain, but only merely as pressure sensations. Later, the affected parts become swollen, cyanotic, bluish-red and congested. If this circulatory stasis does not abate, then gangrene occurs. The fingers and toes may become totally gangrenous whilst proximally merely the superficial tissue layers are involved.

A rather characteristic type of gangrene is that involving the heel, and when this type is more extensive, the larger part of the sole of the foot becomes gangrenous.

In certain instances, smaller or larger areas of skin and subcutaneous tissue of varying size over the shin bone, or in fact, over any portion of the leg may become frozen as the result of exposure in wet stockings or large indolent ulcers may result.

Clinical Course.—The following clinical picture is described by Volk and Stiefler.¹ The affected extremity is swollen, exceedingly painful, and temperature may accompany the local phenomena. The skin is livid and bluish and is lifted up here and there into large blebs or is easily cast off. Subsequently, extensive gangrene of the distal parts occurs, particularly when anesthesia has lasted for a few days. In the severe cases of freezing necrosis of the superficial tissues, involving muscles and tendons, and even mummification or moist gangrene of the fingers, toes or a portion of the foot may occur. Spontaneous amputation has been noted, and erosion into the large vessels may take place. Some authors² describe the occurrence of a moccasin-like gangrene involving the sole and big toe of the foot.

Rather characteristic features are the implications of the heel, and the freezing of the finger tips *without* involvement of the thumb. Meyer and Kohlschütter³ describe typical pictures where the tips of all the fingers are frozen, ulcerate or become gangrenous, the thumb often remaining free.

Regarding the symptoms of pain when parts are frozen, authors vary considerably. Zuckerkindl reports cases in which mortification of the affected part can occur *without pain*. Patients may have no knowledge of the state of the parts until, after removal of the shoes, the condition becomes manifest. In such cases spontaneous pain begins only then when the superficial blebs are opened, and the corium becomes exposed to the air. Other authors, such as Dreyer⁴ report that in the moist gangrene observed during the Balkan war, pain appeared as a late symptom and was followed after seventy-two hours by swelling and gangrene.

Still others have observed that practically all patients have subjective manifestations in the affected territory complaining of paresthesiæ such as feeling of numbness, a wooden feeling, stiffness, prickling, formication, burning and sensations of heat and cold.

About one-third of the cases under the observation of these authors developed, what they termed “Erkältungsneuralgie” or neuralgia due to cold. This term was employed to designate a complex of pain in the feet, soles, and

¹ Volk and Stiefler, Wien. klin. Wchnschr., 1915, No. 5.

² Coenen, Thorn, Cilimbaris, Beitr. Kriegsheilkunde, Berlin, J. Springer, 1914.

³ Meyer and Kohlschütter, Deutsch. Ztschr. f. Chir., Bd. 127, March 2, 1914.

⁴ Dreyer, Zentralbl. f. Chir., 1913, Nr. 42.

toes, with tenderness over the anterior tibial and perineal groups of muscles, manifestations that would subside after rest and the use of salicylates. When pain appears shortly or some time after the action of the cold, paresthesiæ were often noted as prodromal signs; these were in no way related in intensity to the degree of the exciting process. Freezing of even moderate degree can evoke intensive paresthesiæ.

Quite in contrast to the sensory phenomena, in cases of ordinary gangrene, these authors observed derangement in sensation over much larger areas and extending much higher than was expected from the extent of tissue injury. Anesthesia may extend well above the line of demarcation (if gangrene occurs) and may be delimited above by a zone of hyperaesthesia.

Etiology.—It is known that a reduction of temperature down to the freezing point of blood or below is not necessary to bring about what is known as freezing of the tissues; but that temperatures even above zero centigrade suffice provided that predisposing factors are at hand. Indeed gangrene may take place at a temperature considerably above the freezing point of blood (even 6° to 8° C.).

Such predisposing factors are firstly, moisture (wetness); secondly, local; and thirdly, general predisposition, these including all the noxious factors that may lead to ischemia of the vessels. Whilst reduction of temperature of any part of the body through the action of cold air takes place by radiation, chilling of the body by reason of moist cold, such as wet clothing and snow, takes place more rapidly through direct conduction. The most dangerous degree of cold is at the thaw and melting point. It has been noted by Sticker that most cases of freezing during the Great War occurred during the time when the snow began to melt.

Local predisposition is still further conducive. Thus, the distal parts of the body are most prone to become frozen, especially parts that are least well provided with blood. A disproportion between the surface extent and the volume of a part is another factor that makes fingers, toes and ears susceptible.

Loss of heat is greater when the air is in motion. The presence of bodies of good conductivity, such as metal, is dangerous. Water, too, is to be feared when in direct contact with the skin. Those portions of the body which are not only exposed to cold, but suffer impairment of circulation through restricted motion, and constriction of the circulation are particularly sensitive to gangrene. The deleterious effects of tight shoes, shrunken and wet boots, and tight and wet stockings are well known.

Internal causes are bodily weakness and disease. These minimize the body's protecting forces. Lack of power of adaptation to surroundings is a predisposing cause. Thus, individuals who are able to withstand unusual climatic changes including exposure to moisture and cold are less susceptible to gangrene. A certain amount of resistance can be acquired gradually through artificial exercises. Statistics demonstrate that most cases of gangrene of this type occur in the autumn, whilst later in the season, when a certain degree of adaptation (acclimatization) has become possible, its incidence diminishes.

Patients that have just recovered from a malady are also susceptible; which is in keeping with the frequency of gangrene in post-typhoid and in cholera cases.

Pathogenesis. *Direct Tissue Injury.*—Life is dependent upon the continuance of definite temperature in the protoplasm. There are upper as well as lower limits under which it can no longer continue. The lower limits vary

considerably in different animals. In man and many of the warm blooded animals 25° C. is considered incompatible with existence. The circulating blood usually causes renewal of warmth. With impairment of circulatory activity, however, the two factors may combine to exert a deleterious result.

The direct effect of cold, from the physical standpoint, is a change in the colloid solution of the protoplasm. Within certain limits it is rather the duration of the lowering of temperature than the degree that is important, so standing in cold water for many hours leads to gangrene, whilst freezing with the ethylchlorid spray for several seconds does not. It has been shown by Schade that the elasticity of the tissues may return to normal when the loss of warmth lasts but a short time. In addition to the changes in the colloids, chemical changes occur—changes in the crystalloid solution.

The Effect of Freezing in This Type of Gangrene.—The temperature of 0° C. does not indicate a critical point. *In vitro* the blood and human fluid freeze at a temperature of -0.66° C. but in the body a much lower temperature is necessary. With the formation of ice, however, an additionally injurious factor is added. Freezing is only of significance in that a rapid and intensive loss of water is occasioned thereby. It is well known that plants that have been frozen show macroscopically and microscopically the same appearance as dried ones. Indeed, those forms of life that are not dependent upon water cannot die by reason of cold.

Experiments have shown that with a marked lowering of temperature, an alteration of the protoplasm from the *sol* condition into the *gel* condition takes place; that is, the substances in solution approach the precipitate or solid state. The body cells do not possess the same characteristics or qualities at a temperature of 20° that they do at 30° C. The microscopic examination, however, does not always show corresponding changes. The elasto-metric method of Schade is a new procedure for the investigation and demonstration of this subject. In a specially constructed apparatus, this author showed that elasticity of the subcutaneous tissues diminished in a state of fatigue, general disease, and local cold, even though the fluid contents did not change. Elasticity is the quality or capacity for alteration of form and return to a previous state. A measureable loss of elasticity can take place in fat-free tissues only through a change in the physical condition of tissues, namely, in their protein substances.

After return to normal temperature, the disturbance in the colloid mixtures does not cease when the degree of what is known as “reversible” has been exceeded.

The formation of ice in the tissues is another deleterious factor. As a matter of fact, the whole watery solution of colloids and crystalloids which we recognize as the fluid protoplasm, the lymph and the blood plasma, does not become converted into ice. The ice formation takes place in the precipitation or congealing of pure water in a solid form out of the tissues, with simultaneous concentration of the remaining solution. By virtue of the higher concentration of the colloids themselves, and particularly the crystalloid substances, the transference of the colloids into their *gel* condition is intensified. At the same time carbon dioxid and oxygen previously held in by the water become free. The microscopic pictures noted in frozen ameba bear out this view.

For the living cell therefore, freezing exerts its influence by virtue of a rapid and intensive withdrawal of water. And, furthermore, forms of life which we regard as latent, do not appear to suffer from cold. The time factor is important because the changes are slow. After a certain lapse of minutes, a portion of the cell protoplasm becomes converted into the *gel* condition so that the remainder does not suffice.

The alterations in the protein substances are not reversible after long periods of freezing. This corresponds to the condition of frozen solutions of devitalized colloid substances, such as egg albumin which, even after being thawed, show their spongy structure, and do not return to their *sol* condition. These changes are the same for all degrees of temperature and the time required for annihilation of life varies. When the human skin is frozen with ethyl chlorid for from one to two minutes, it is assumed that during this period, an adequate portion of the protoplasm retains its *sol* condition, and can subsequently resume its vital function. Thus, some animals can withstand freezing for longer periods of time. It has been shown that medusae can remain frozen for hours.

The manner of thawing does not seem to be as important as is believed. Clinically, acute gangrene does not ensue immediately after exposure to cold. The rôle of the blood vessels seems to be an important one.

The Rôle of the Blood Vessels.—Authors are at variance, as to whether in gangrene due to cold (freezing) the reduction of temperature per se, or the cessation of circulation plays the greater rôle. Wieting¹ and Marchand² have applied the word "ischemic" (Kälte-Gangrän) to this variety. According to this view the thermic influence produces a spastic contraction of the arteries, even to the extent of complete obliteration of their lumina. And because this effect may last for a considerable period of time, and other predisposing factors are at work, gangrene is the issue. Wieting believes that a vessel palsy together with true impairment of the vascular innervation, is an important activating factor, for with it go stasis and thrombosis.

From what has been said it is clear that immediate action of withdrawal of heat from the protoplasm plays an important part in the production of gangrene due to cold, but it is not the only cause. The blood carries renewed calories to the refrigerated tissues, and it is only when the loss of heat preponderates over that which is received that injury to the tissues sets in.

When the action of cold is very intensive, a deleterious result is obtained, even if the vascular system functionates with normal or accelerated activity.

It is generally believed that contraction of the blood vessels follows stimulation by cold. If contraction of the vessels were the only and regular reaction on exposure to cold, the condition of gangrene due to cold would be adequately explained. Loss of warmth without substitution, absence of oxygen and nutrition would act similarly in bringing about cell death.

Marchand³ holds this view when he says that the anemia produced by contraction of the small vessels can become complete and can thus lead to death of affected parts. However, as a rule, the reaction of the blood vessels is somewhat more complicated.

The first sequence of the action of cold water is, indeed, a contraction of all of the vessels in the affected parts, including arteries as well as capillaries and veins. The skin becomes pale and the extremities lose in volume. This condition may persist for some time in anemic individuals, the part remaining pale and cold, rigid, and permanent injury to the parts may ensue. In anemic people as a result of mere contraction of the blood vessels, death of tissue in the sense of an ischemic gangrene may eventuate.

The cases in which gangrene occurs immediately after exposure to cold are relatively rare. Usually, days, weeks or months intervene before the injured tissues die off. Doubtlessly the condition of the blood vessels is responsible. To explain the delayed mortification, the question has been put as to whether the tissues are not found in a condition of diminished vital energy after the action of cold; also as to whether limited portions of tissues or cells can be injured or comparatively devitalized in the multicellular organisms and remain in such a state even after the causal agent has ceased to be active. Histologic and biologic observations, however, do not seem to lend acceptance to the view that single cells can remain in a state of permanent deterioration or devitalization, in a multicellular organism. Indeed, it seems rather more plausible that when such permanent or protracted local morbidity exists, lesions in the blood vessels are at fault.

Animal experimentation has shown that the vessels may permanently contract as the result of the action of cold. When the extremities and ears of rabbits were put into a cold solution at 20° below 0° C., they were found to remain bloodless until freezing took place. When the same cold mixture was brought into contact with the femoral arteries, so intensive a contraction was obtained, that no blood passed through it (Catiano⁴). In healthy individuals and under atmospheric conditions in which adaption has taken place, a dilata-

¹ Wieting, *Centralbl. f. Chir.*, 1913, p. 593.

² Marchand, *Krehl-Marchand, Handb. d. allg. Path.*, 1908, I, p. 114.

³ Marchand, *Handb. d. allg. Path.*, 1908, Bd. I, also 1912, Bd. II.

⁴ Catiano, *Langenbecks Archiv.*, 1883, Bd. 28.

tion of the vessels follows sooner or later. Further investigation has shown that transitory reduction of temperature of an artery is followed by immediate contraction, but after a few minutes circulation is restored, and the vessel dilates beyond its original calibre. Even when cold is applied for a longer period of time it is found that in the frog after preliminary vasoconstriction, dilatation takes place beyond the normal, and whilst the cold is still in action. After restoration of the external temperature, the vasodilatation may continue for from ten to twenty minutes or more (Sartorius¹). In the case of the rabbit, too, when cold acts slowly, excessive dilatation may occur after preliminary contraction, and persist for many hours, even though the snow be still in contact. It is believed that this reaction of vasodilatation takes place whenever the organism has become accustomed to severe and excessive fluctuations of temperature. That this is true, experimental observations attests, whilst the unexposed portions of the body, such as the mesentery or internal organs, manifest none of the above reactive phenomena.

We know that the face and hands become pale as the direct effect of cold, but subsequently flush if the individual is accustomed to cold and is in good health. In chronic disease, and in anaemic people, the reactionary reddening may not take place. The nude body, when exposed to cold and wind, may remain pale, with the surface vessels contracted whilst the skin of the face that is used to exposure, may react with a marked flushing. These well known phenomena of reactive hyperemia following cold are of importance. They should be borne in mind in prophylaxis. For, when the reactive dilatation is adequate, even severe degrees of cold fail to bring about gangrene. The factors that constitute the closing links in the chain of deleterious moments, and to which the gangrenous outcome is greatly due, may be summed up as follows.

Firstly there may be an inadequate adaptation of the vascular system. Since the reaction of the vessels is intensified and prolonged through exercise, and climatic experiences, an absence of the latter would conduce to inadequate or insufficiently long dilatation, and subsequent vasoconstriction. In such circumstances the influence of cold, would bring about total plasmic changes and necroses, both by virtue of the action of the cold itself, as well as through the insufficient oxygenation and nutritive supply. This explains the observation that soldiers are better able to withstand the cold and wet during the winter or early spring, than in the fall.

Secondly, disease and weakness may cause the absence of insufficient reaction. Such individuals are unable to deliver as much blood and as many calories as are necessary for the conservation of any particular portion of the body when threatened. Gangrene due to freezing also was noticed more often when the extremities had been injured by bullet wounds, than when intact.

Thirdly, tight body coverings, shoes, stockinettes, stockings, etc., may cause ischemia and constriction of the vessels by interfering with adequate reactive vascular dilatation. There must be enough room to accommodate the increased volume incident upon the dilatation of the vessels.

The Effect of Stasis.—When the action of cold is prolonged and does not directly lead to freezing, the dilatation of the vessels loses its reactive nature. Whilst, it is ordinarily superseded by vasoconstriction, it would under such circumstances induce marked congestive dilatation of the capillaries.

The flow of blood would become slower until the circulation finally ceases. The skin then takes on a bluish red or crimson red discoloration and edema of the tissues follows. Then blebs form. There is loss of the active muscular power, and loss of sensibility. In such a case, tissue death sets in and, after a time, macroscopic evidences of gangrene in the dry or in putrid wet stages, make their appearance. The important observations in this

¹ Sartorius, Inaug. Diss., Bonn, 1864.

respect are those which have demonstrated that with a certain degree of tissue injury, the blood flow ceases in the dilated capillaries, although the afferent and efferent paths are open. Coagulation does not appear to occur at first, which is in keeping with the fact that occasionally the circulation can be again restored. This so-called stasis with interruption of circulation has not been altogether explained mechanically. This much, however, may be said, that when the tissue injury or insult has attained a certain degree, the blood ceases to circulate through the affected territory. This applies not only for the chemical or caustic injuries, but also for refrigeration. In the case of congelation it is probable that the tissue degeneration is the most important effect of freezing, whilst the circulatory disturbances and the stasis are accompanying and secondary. When stasis occurs, tissue death is predestined.

The Importance of Vessel Palsy.—A number of authors have attributed death of the tissues from cold to paralysis of the blood vessels. Wieting¹ thinks that the essential factor in cases of protracted action of cold is the paralysis of the vessels which is occasioned by injury to the vascular innervation, and is followed by stasis and thrombosis. For this reason he speaks of the necroses occurring during the Balkan War as paralytic vessel gangrene, (neuroparalytic) gangrene of the vascular paralytic type (Marchand).² Reference will be made on pp. 571 and 578 to the history of previous effects of cold in some of the cases observed.

Both endarteritis and thrombosis have been considered as the causal factors, when the action of cold precedes the mortifying process by weeks or months. Indeed, it is assumed that the vessel endothelium is exceedingly susceptible to the action of cold.

A number of authors in experimenting with the action of ether spray on vessels found that degeneration of the media and consequent proliferation of the intima with narrowing of the lumen took place.³ It is interesting to note not only the immediate degenerative phenomena but the late proliferative condition of the endothelium. This suggests that the lesion is a replacement phenomenon, with substitution for the cells that had been destroyed (cicatricial in nature). The consequent narrowing of the lumina of the arteries is held responsible by some for the late gangrene. The eventual mortification is said to occur either by reason of the gradual impairment of circulation, or may ensue in such poorly nourished territories, whenever a secondary insult still further jeopardizes the circulation.

Thrombosis.—Thrombosis is regarded as a rare cause of gangrene after freezing. Observation of experimenters along these lines, however, has shown that arteries dissected free and exposed to the strongest and severest degrees of cooling contained fluid blood so long as the vasoconstriction was insufficient to well nigh obliterate the lumen. Uschinski⁴ could demonstrate thrombi only in some of the veins.

There are three cases found in the literature in which extensive thrombosis occurred after freezing. One of these was reported by von Recklinghausen⁵ in a woman whose feet were frozen, and in whom the veins leading to the gangrenous toes were found thrombosed. Von Winiwarter⁶ described a case of widely distributed arterial thrombosis in a man who had been exposed to cold. Nägelsbach⁷ described a case in which all of the large arteries of the foot and leg were thrombosed after freezing. It would appear

¹ Wieting, Zentralbl. f. Chir., 1913, p. 593, p. 1985.

² Marchand, Handb. d. allg. Path., 1908, Bd. 1.

³ Zoege v. Manteuffel, Zentralbl. f. Chir., 1902, 3.

⁴ Uschinski, Ziegler's Beitr., 1893, p. 115.

⁵ Recklinghausen, Deutsch. Chir. Lief. 2 and 3.

⁶ Von Winiwarter, Langb. Arch., 1879, Bd. 23, p. 202.

⁷ Nägelsbach, München. med. Wchnschr., 1919, p. 353.

therefore that although thrombosis may occur after freezing, it is a rather rare cause of gangrene.

Prognosis.—Opinions vary as to the criteria according to which a prognosis of the viability of a part subjected to cold is to be based. A persistence of pallor, coldness, lividity and anesthesia, has been regarded as of valuable prognostic significance. Certain authors (Meyer and Kohlschütter¹) believe that if spots of cyanosis, lividity and areas of anesthesia are present after a week, the affected part cannot be expected to recover. Other authors suggest the making of minute incisions in order to determine whether well oxygenated blood trickles forth from the wound. It has been suggested to apply the Moskowicz test. This in our opinion, would be contraindicated because of the danger of inducing thrombosis and vessel injury.

Therapy of Local Freezing.—Calcium salts, (particularly calcium lactate) because of their influence on the phagocytic power of the leukocytes and their stimulation of connective tissue formation, have been suggested as a means



FIG. 44.—Multiple incisions for the prevention of gangrene. (H. Flörcken.)

of combating the effects of freezing. In freezing of the third degree, it has been traditionally accepted that the thawing or warming should take place as slowly as possible. This does not pertain merely to cases of actual freezing, but also where the reduction of temperature has been less intensive. Cases of extensive gangrene are reported, and the occurrence of this complication is attributed to sudden change of temperature. Some authors suggest rubbing with snow, others, such as Bundschuh,² employ cold water for almost an hour until the bath reaches the body temperature. If the frozen part regains its sensation and becomes red, minor lesions of the tissues may be prognosticated. When anesthesia and pallor persist, massage is recommended. Other authors recommend massage over long periods of time, continuing over twenty-four hours in half hour intervals. Kroh³ is said to have revived extremities that presented all signs of impending gangrene.

Other authors use the hyperemia treatment with or without baking. Elevation of the affected extremity is advised by Sonnenburg and Tschmarke.⁴

¹ Meyer and Kohlschütter, *Deutsch. Ztschr. f. Chir.*, March, 1914, 127.

² Bundschuh, *München. med. Wchnschr.*, 1915, No. 12.

³ Kroh, *Cit. by Flörcken, Ergeb. d. Chir. u. Orthop.*, 1920, Bd. 12, p. 202.

⁴ Sonnenburg and Tschmarke, *Die Verbrennung u. d. Erfrierung*, Ferd. Enke, Stuttgart, 1915.

Multiple incisions are regarded as of great value where the return venous circulation is impeded and are said to have been the determining factor in the saving of many limbs threatened by gangrene (Noesske,¹ Wieting²).

When the greater portion of the peripheral phalanges, is frozen, Bundschuh makes multiple incisions over the ventral and dorsal aspects of the phalanges. The schematic drawing (see Fig. 44) shows the situation of such incisions. The hyperemic treatment with elevation has been combined with this method. Other authors recommend the use of quartz light subsequent to the making of the incisions. Alternating hot and cold baths have also been suggested.

It has been recommended by various writers that an effort should be made to convert moist gangrene into dry gangrene, and to this end the removal of the detached epidermis (Strohmeyer) has been advised. The application of dry dressings and powders, such as dermatol, finely pulverized charcoal and similar preparations, with or without the use of dry heat is frequently followed by good results. Even X-ray treatment (Wachtel³) is said to have been of service.

Operative Treatment.—Conservatism is the watchword, and should be followed wherever possible. One should not be too hasty in pronouncing judgment regarding the eventual outcome, and operation should be deferred when one is in doubt. Early amputation is only then indicated, when complicating infection with phlegmon formation is imminent; or, when the septic resorption from a typical gangrenous territory serves as indication.

Whilst the larger number of surgeons urge conservative therapy wherever possible, waiting for a line of demarcation to form and for sequestration to take place spontaneously, others lay great stress upon the advisability of obtaining a valuable functional stump. The latter proceed shortly after demarcation has become established, to the surgical measures that will assure such an issue.

CHAPTER XXXII

GANGRENE DUE TO CHEMICALS AND DRUGS

Certain chemicals or drugs taken internally and applied locally may cause gangrene. Ergot, although not taken in the form of a drug, may be considered here as one of those substances that may produce gangrene when taken internally. Mercury, orthoform, phosphorus, carbolic acid, trichloroacetic acid, strong acids and alkalies, may produce gangrene under certain conditions.

The action of chemicals on cells and tissues is of manifold variety. They may combine with the proteids of the protoplasm and form more solid combinations; or effect coagulation, dissolution and precipitation; or alter especially the colloids; or have an affinity for certain tissue constituents causing solution of lipoids and thereby destroying the construction of the cells. Poisons do not act like nutritive substances in proportion to their

¹ Noesske, Chir. Kong., 1920, Stuttgart.

² Wieting, Zentralbl. f. Chir., 1913 Nos. 16 and 52.

³ Wachtel, Wien. klin. Wchnschr., 1917, No. 18.

caloric value. They resemble rather the catalytic ferments in that they become the exciting factor in the mutation of normal stresses or forces, or exert a sort of restraining (paralytic) action on the normal processes. There does not seem to be any relation between poisonous activity and atomic weight, but rather some conformity with their valency. Varying effects may follow the application of one and the same substance according to its concentration; namely, stimulant, or paralyzing in weak solutions, inflammatory or suppurative in stronger concentration, or even with capacity for causing necrosis or gangrene.

The source of these poisons may be the mineral, plant or animal kingdom. To these may be added those produced by pathogenic and saprophytic organisms, and those synthetically made up. Examples are arsenic, lead, mercury, and barium; of alkaloids, glycosides, proteins, toxalbuminates, enzymes, bacteria, and alien (heterologous) blood, (such as causes hemolysis, agglutination or precipitation).

Substances that irritate the tissues severely may produce inflammation, suppuration or necrosis. Such are acids, alkalies, alkaline salts, metals, nitrogenous bodies and the irritating combinations of organic compounds. All acids have varying degrees of caustic action locally, according to the quantity applied and the concentration. When the cells are killed off, *direct* necrosis, gangrene or mortification ensues. Even weak solutions (about 5 per cent of muriatic, nitric or sulphuric acid, and caustic potash), may produce gangrene when applied as moist compresses for 20 to 24 hours. These drugs lead to maceration of the epidermis, necrosis, the deeper tissues becoming subsequently affected. Trichloroacetic acid is also dangerous, if it be incorrectly used in the form of a wet dressing, when applied to remove surface warts.

Sulphuric acid causes coagulation of albuminous substances of the tissues through withdrawal of water and heat production. The black eschars occasioned by it, however, are not expressions of carbonization, but due to the presence of derivants of blood pigment, such as hematin, acid methemoglobin and hematoporphyrin.

Nitric acid (over 33 per cent solution) causes immediate brownish-yellow discoloration. Proteids are precipitated by nitrification and changed into xanthoproteinic acid. There occurs coagulation of the blood in the vessels of the territory affected.

Chromic acid also precipitates in its local action, its salts causing oxidation of cells. A greenish discoloration may result.

Oxalic acid is caustic and dissolves collagenous tissues.

Formalin or formaldehyde roughens the skin, hardens it, and brings about coagulation of albumin, having caustic and necrosing action on mucous membrane when sufficiently concentrated.

In short, the acid group are caustics that may effect rapid disorganization of the protoplasm. This eventuality may be the result of withdrawal of water (sulphuric acid), albuminous precipitation (organic and inorganic salts, fatty acids, trichloroacetic acid), or through salt combinations with proteids (acid albumins).

The halogens destroy the protoplasmic structure, in that they take up water and thus make salts that precipitate proteids. *Chlorine* and *fluorine* have the strongest action. *Hydrochloric acid* may lead to ischemic necrosis of the skin. So also chromic acid combinations may produce necrosis.

The alkalies are not unlike the acids in their effects. However, these are characterized by the development of soft, smeary shreds of swollen disin-

tegrated tissue—a true example of their dissolving effect (also called colliquation or colliquation necrosis).

Arsenic may have a caustic action in its oxidizing powers.

Phosphorous is especially dangerous for its peculiar necrotizing effect on the jawbone, and there may even occur involvement of the vomer and sphenoid. These are the sequences of the inhalation of phosphorous fumes in the manufacture of matches. Of the *mercurial* poisons calomel is a weak bichloride (sublimate) of mercury, an intensive caustic. The oxide, chloride and iodides combine locally at the site of application with the proteids, causing death and destruction of the cells. *Mercury* is reported to produce local sloughing at the site of injection, gangrenous patches in the gastro-intestinal tract, and sloughing of the skin.

Silver nitrate combines with the proteids of the tissues to form a silver albuminate, appearing as whitish eschars that become dark through the action of light. In the blood this salt exerts a specific action on nerve cells, causing spinal paralyses, temporary paresis, paralysis of the vasomotor centers and of the respiratory center.

Although caustic effects have been noted in the stomach from the contact of *lead*, this poison is of no special significance as a clinical factor in the production of necrosis. The same may be said of zinc and copper.

Local necrosis has resulted from the subcutaneous injection of the *poison of bees and wasps*. *Serpent venom*, too, has produced gangrene (in case of the crotalidae).

Finally, we may mention the distinctive effects of some of the microbic poisons. Tuberculin (old) and mallein in concentrated form may bring about necrosis. Substances of similar action have been derived from the bacillus pyocyaneus, prodigiosus, proteus and penicillium glaucum. Cell necrosis, too, may follow the action of *ectotoxins*.

The bodies of bacteria *endotoxins* have similar effects.

A gangrenous form of eruption is recorded in the literature as following the use of *orthoform*. Gangrenous patches and ulcerations are said to complicate the use of this drug about the fingers, anus and nipples.

Carbolic Acid Gangrene.—The fingers or toes are usually affected following the local application of ointments or wet dressings. The gangrene may result after the application of even a very weak solution (such as 0.5, 1 or 2 per cent). After the dressing has been applied for a few hours, the finger or part becomes blanched, and a pricking sensation is felt. Within 24 hours or less, the skin becomes dusky, discolored, dry gangrene may occur, the part becoming gradually mummified.

Various theories have been offered to explain the cause of gangrene from the use of weak solutions of carbolic acid. According to one view, thrombosis is produced in the peripheral vessels; according to another, a particular action upon the trophic functions and vascular nerves is exerted.

Amputation is advisable according to the view of Leclerc¹ who bases his conclusion on the following observation.

A woman 50 years old, despite the fact that she was given accurate proportions for a phenol dressing, to be applied to the finger, applied a compress saturated with the pure solution for 24 hours without any sensation of pain. Upon removal of the dressing the finger was found dead white, shriveled, and at the end of 6 days it became gangrenous. Two days later pain of the hand was experienced and "erythema" on the back of the hand developed. Symptoms of disturbed mentality now followed, with extension of the gangrene, and the following day elevation of temperature (38° in the morning and 38.3° in the evening) and pulse 140. Then came a state of collapse and exitus on the following day.

¹ Leclerc, Bull. de l'Acad. de méd., Paris, Feb. 25, 1919, 81, 205.

Lysol, too, may be regarded as dangerous in solutions that are not thoroughly mixed, as the case of Sowles¹ demonstrated.

In a patient who soaked his right index finger over a total period of about 15 minutes in a basin of water, into which an "indefinite amount" of *lysol* had been admixed, the distal half of the finger became intensely swollen the following day. Examination, 24 hours later, demonstrated marked redness and swelling with a sharp line of demarcation. The epidermis of the dorsal distal half of the finger was white and raised from the subcutaneous tissue, appearing to be dislodged by serum or pus. However, on removal of the dead skin, the subcutaneous tissues were evidently dry and gangrenous.

In the following case observed by von Stapelmohr² the agent was a 5 per cent solution of *lysol*.

A woman of 53 had cut her left thumb 4 days before coming to the clinic. Two days after the accident she had wrapped her thumb in a *lysol* drenched bandage for 12 hours, and later had held the thumb for 2 hours in the same 5 per cent *lysol* solution.

Upon examination the skin was slightly red with occasional small blisters. In the next few days the terminal phalanx became black, and 11 days after the injury the finger was amputated, at which time the soft parts were also attacked by dry gangrene.

Gangrene Due to Poisonous Gases.—Thrombosis in both deep and superficial vessels (veins) may succeed the inhalation of a number of different toxic fumes and gases. As examples of such we may quote some of the records of gangrene due to *carbon monoxid* and *illuminating gas*. After exposure to carbon monoxid from a charcoal stove, the following condition is reported as having resulted in one case (Thandavaroyan³).

Areas of hyperemia were observed confined entirely to the left side of the face, left hand, lower part of the chest and left thigh. Although the hyperemic areas on the face and chest disappeared after a few days, raised anesthetic areas appeared on the left hand and thigh. Four days later gangrene of the little finger of the left hand set in, with absence of circulation in the other fingers of that hand. The dry gangrene was well demarcated; the swelling of the hand and thigh improved under treatment; amputation was refused.

Briggs⁴ relates this instance.

After accidental disconnection of a pipe line on a motor boat unbeknown to the patient, he retired to his cabin, where he was soon after found unconscious.

Upon examination it was found that the backs of both hands and feet were covered with large tense blebs. In spite of conservative treatment, extensive gangrene of both upper and lower extremities rapidly developed, and on January 24, 1919 his condition was as follows.

Right hand—gangrene of the entire three middle fingers, inner border of the thumb and little finger.

Left hand—gangrene of the distal phalanges of the four fingers and flexor surface of the thumb.

Right leg—gangrene over outer border of tibial region, external malleolus, outer border of dorsum of foot and small patches on three toes.

Left foot—gangrene of two toes.

The necrosis attacked the skin, muscle tissue, tendon, periosteum and bone, as also several joints.

January 28, 1919 (37 days after the accident) amputation of the following members was performed. Right-hand—disarticulation of 3 fingers; left hand—4 fingers.

Riedel⁵ reports a case of gangrene of the leg after *illuminating gas poisoning*.

Several days after an attempted suicide with illuminating gas a woman was attacked by nausea, abdominal pains and stiffness of both legs attended with pain in the legs. After 7 days the posterior tibial and anterior tibial arteries became thrombosed (probably as the result of the prolonged retention of carbon monoxid in the blood).

¹ Sowles, Boston Med. & Surg. Jour., 1919, p. 510.

² von Stapelmohr, Hygeia, 1917, 79, 438.

³ Thandavaroyan, Lancet, April 30, 1921, I, 910.

⁴ Briggs, Jour. Am. Med. Assn., Aug. 30, 1910, 73, 678.

⁵ Riedel, Deutsch. med. Wchnschr., June 9, 1921, 47, 651.

Gangrene Following the Injection of Medicaments.—A few examples of gangrene following hypodermatic or subcutaneous injection of adrenalin, arsphenamin, quinine, and after simple hypodermoclysis, may suffice to illustrate.

Following injection of glucose solution with adrenalin, Guilera¹ reports a case.

A primipara of 23 years after receiving 2 injections of 350 grams of glucose solution with adrenalin into the right thigh developed a gangrenous area. The necrosed zones were extirpated and the dead tissue removed "en bloc" down to the aponeurosis.

In this case the gangrene was not due to the volume of the liquid injected nor to any defect in preparation of the solution, or in the technic of the injection. The writer attributes it to the vasoconstrictive action of the adrenalin contained in the glucose serum in an anemic, infected person.

Muller² reports gangrene after subcutaneous injection of *sodium chlorid*.

Because of post-partum hemorrhage in a female 29 years of age, 1000 cc. sodium chlorid solution were injected subcutaneously into the thigh. Two days later about 20 cm. from the site of injection the skin of both thighs became dark blue and blistered. Gangrene spread rapidly. The patient left the clinic unrelieved.

In explanation of the gangrene the author believes a chemical effect could be ruled out inasmuch as the solution was made up correctly; that a thermal injury was not responsible, inasmuch as the temperature was controlled, and was in reality too cold (35°); that no bacteria which might cause the infection were found at 37.4°; and further, that injection into the fascia (which Jungmann believes to be an important cause of gangrene following sodium chlorid injection) did not occur in this case. The only remaining etiological factor could have been the pressure necrosis such as is described by Liepmann. This is caused by delayed resorption and consequent prolonged pressure effect upon the surrounding tissue and capillaries.

Gangrene Following Injection of Quinin.—According to Prat, Flottes and Violle³ quinine necrosis is exemplified by the following report. The patient received about 10 aseptic injections of chlorhydrate of quinine into the gluteal region, and after about 2 weeks a small focus of induration was observed. Three to 4 days later the region began to swell, the skin became stretched without reddening, and sensitive to pressure, soon resulting in a deep mass.

If an incision be made in such a case at this period, necrotic tissue is exposed. The quinine determines an amicrobic mortification, an aseptic necrosis of the tissues. The cellular tissue is the most altered, the skin intact. The muscles are changed later; groups of fascia become indurated and mortified; veritable blocks of necrosed fibers are easily detached from the healthy muscle fascia. Finally the cellular tissue is filled with pus and the skin drops off in gangrenous shreds.

Left to itself, quinine necrosis would end in sphaceli, extensive detachment and bacterial suppuration. In the "quinine abscess" globules of pus, degenerated leukocytes, pyogenic microbes, blood corpuscles and fatty granulations are observed. The formidable decay of quinine necrosis generally necessitates surgical intervention under chloroform anesthesia. This consists in wide and deep incisions, going beyond the limits of the affection and excision of the mortified tissues.

Sutter⁴ records gangrene of the fingers due to the **injection of arsphenamin**.

¹ Guilera, Rev. espan. de med. y cirug., Barcelona, 1919, 2, 664.

² Muller, Med. Klin., Aug. 1, 1920, 16, 804.

³ Prat, Flottes and Violle, Bull. de l'Acad. de Paris, April 10, 1917, 77, 506.

⁴ Sutter, Jour. Am. Med. Assn., Nov. 22, 1919, 73, 1611.

In case O. P. M., aged 35, immediately after the injection of 0.4 arsphenamin diluted in 250 cc. of normal salt solution, into a vein of the left arm, there was severe pain in the hand and the peripheral circulation was poor. According to the history there was evidently some infiltration about the site of the intravenous injection. Subsequently dry gangrene of the distal portion of all the fingers took place, the index finger being involved up to the middle phalanx, and the middle finger to a somewhat less degree, the ring finger up to the middle of the second phalanx. Amputation of the thumb distal to the first phalanx, of the index finger 1 cm. proximal to the middle phalangeal joint, disarticulation at the middle phalangeal joint of the middle finger, and of the middle phalangeal joint of the ring finger were carried out approximately 3 months after the injection of arsphenamin.

Gangrene Due to Ergot.—This results from eating bread made of spurred rye, and has not been observed when ergot is taken for medicinal purposes. This disease was not uncommon in the eighteenth and early part of the nineteenth centuries, particularly in Europe, where epidemics of so-called ergotism are known to have occurred. At present it occurs but rarely, and then only sporadically. Two types are described, a *convulsive* and a *gangrenous* type, although both types may be combined.

After prodromal gastro-intestinal disturbances, such as diarrhea, colic, occasional vomiting, disturbances of the circulatory and nervous systems appear. The extremities may become cold, numb, blue; the pulses may become weak and muscular spasms may occur. When the spasms become more general, seizures of an epileptic nature develop. In the gangrenous type of case, either the toes or fingers are usually affected. They become cold painful, show cyanotic or purplish patches which gradually mortify, gangrene being usually of the dry type.

Cases described as occurring in southern Russia are said to begin with formication, coldness, numbness of the fingers and toes, gradually resulting in bluish black discoloration, drying and detachment of nails with necrosis of parts or whole fingers or toes. Either dry or moist gangrene may affect the peripheral parts, including even the nose and the ears, and may be accompanied by severe pain that disappears with sequestration of the tissues. In the mild cases small islets of epidermis only are separated, or blebs appear and the hairs fall out. The gangrenous blebs are analogous to those of herpes zoster gangrenosa.

At other times the malady may remain latent until an intercurrent disease such as pneumonia, scarlet, typhoid, and so forth activates it. Then severe lesions, such as gangrene of the lung, skin, intestines and of the female sexual organs, may develop.

The three chief actions of ergot, namely, its spastic influence, uterine stimulation and production of gangrene have been referred to three different toxic elements; the first, to ergotin and ergotoxin; the second to ρ hydroxyphenylacthylamin; and the third to sphacelinic acid and to sphaceotoxin (Kobert's appellation, *sphacelinic acid* so derived from the Greek word *sphakelos* meaning gangrene). Other authors, however, ascribe this action to an amorphous alkaloid "ergotoxin." The preparation of Kobert¹ is effective on the peripheral parts, when diluted solutions are taken internally; while in concentrated form it causes necrosis at the site of application—pharynx, and gastro-intestinal canal. Even fowl (especially the cock) when fed with ergot show symptoms, and the tips of the cock's comb are reported as showing necrosis as well as the tongue and wings.^{2,3} Von

¹ Kobert, Arch. f. exper. Path., XVIII, 1884; also Lehrbuch der Intoxikationen, Stuttgart, 1906.

² Grünfeld, Arb. d. pharmak. Inst. z. Dorpat, XI, 1890; VIII, 1892; XII, 1895.

³ Jacoby, Arch. f. exper. Path., XXXIX, 1897.

Recklinghausen found hyaline thrombi in the arterioles, and hyaline degeneration of the vessel walls in the affected regions of these experimental animals.

In explanation of the physiologic action of the poison on the vessels von Recklinghausen offers certain conclusions deducible from his pathologic findings. Noting a ring-like zone of red blood cells between the hyaline vessel wall and the hyaline thrombus, this author concludes that a primary vessel contraction, attended with stasis and hyaline thrombosis of the contents, is followed by relaxation, dilatation of the vessel allowing a renewed current to be established between clot and vessel wall. According to this theory, the necrosis would be due to the vascular disturbances, and gangrene of this type should more correctly be grouped under the vascular forms. Such a theory would find confirmation in the similarity of the poison's action on the uterine and vascular musculature, on both of which a contractile effect is produced.

CHAPTER XXXIII

MICROBIC GANGRENE

The more important types of *microbic gangrene* are (1) *hospital gangrene*, (2) *noma*, (3) *emphysematous gangrene*, and (4) *gangrene due to virulent pyogenic organisms (streptococci, etc.)*.

1. Hospital gangrene (sloughing phagedena, pulp y gangrene, putrid degeneration, traumatic typhus, nosocomial gangrene) has practically disappeared since modern antiseptic methods have been introduced into surgery, and need, therefore, but slight mention here. It occurred either in epidemics, or was endemic in hospitals, particularly in the military hospitals. Hospital gangrene may be regarded as an acute progressive gangrene with putrid decomposition or degeneration of the wound, initiated by local symptoms, but followed rapidly by severe constitutional manifestations. The cause is doubtless an infectious one, anaerobic bacilli being probably responsible. Matzenauer claims to have isolated a bacillus¹ which however, he could not demonstrate in pure culture. Nasse² found an ameba.

According to the clinical course, authors have described a superficial and a deep form, and according to the external manifestation an ulcerative and a pulpy variety.

Erichsen³ describes the disease as follows. "A disease characterized by a rapidly destructive and spreading ulcer, covering itself as it extends by an adherent slough, and attacking open sores and wounds. When sloughing phagedena invades a wound that is previously perfectly healthy, the surface of the sore becomes covered with gray, soft points of slough, which rapidly extend until the whole of the ulcer is affected. At the same time it increases rapidly in superficial extent, and commonly in depth; the surrounding integument becomes edematous, swollen, and of a vivid red color; the edges of the ulcer are everted, sharp-cut, and assume a circular outline, and its surface is covered with a thick, pulpy, grayish green, tenacious mass, which is so firmly adherent to the sore, that it cannot be wiped off from it, being merely swayed to and

¹ Arch. f. Dermat. u. Syph., Bd. 55.

² Arb. aus von Bergmann's Klinik, 5ter Teil, 1891.

³ Science and Arts of Surgery.

fro when an attempt is made to clean it. There is usually some dirty, yellowish green or brownish discharge, and occasionally some bleeding; the pain is of a severe burning, stinging, and lancinating character, and the fetor from the surface, is considerable. The ravages of the disease when fully developed are extensive. The soft parts, such as the muscles, cellular tissue, and vessels, are transformed into a gray, pulpy mass and the bones are denuded and necrosed."

The diphtheritic form is characterized by certain alterations in previously healthy, granulating wounds. Associated with fever and pain, there appear yellowish-brown areas of discoloration in the granulation, hemorrhages and superficial sloughs. The diphtheritic form may become *ulcerative* when disintegration of the surface takes place. The discolored areas will soon give rise to a foul odor, leave sharply demarcated ulcers which rapidly fuse together, or the bottoms of the ulcers become hemorrhagic and gangrenous, their margins eroded, the neighborhood, tender and painful, and inflamed far beyond the zone of the wound.

The Pulpy Form.—Marked swelling takes place here, gas may develop in the tissues, a mass or pulp being developed, which may be likened to brain substance. Associated with it, extensive hemorrhages may give rise to the hemorrhagic type. In the *superficial form* the process would often be self-limited, whereas in the *deep form* a putrid phlegmon would develop, leading to bone necrosis, even ulceration of vessels, and death due to hemorrhage. Or, the deep form may be associated with toxic general symptoms, that lead to a lethal outcome within two or three days.

As complications, erysipelas, metastatic foci of pus, and lymphangitis have been described.

Treatment.—This consists of the rapid and energetic cauterization of putrid areas with Pacquelin cautery, opening of the abscesses and surgical cleanliness. Sloughs are to be removed, and general stimulants freely administered.

2. Noma.—This form of gangrene, also called *cancrum oris*, *gangrenous stomatitis*, *cancer aquaticus*, is a special form of ulcerative stomatitis with gangrene, that occurs almost exclusively in children between the ages of two and twelve, and often follows some debilitating disease. The affection has its origin in an infiltration of the mucous membrane in the neighborhood of the angle of the mouth. The exudate or infiltration then becomes gangrenous, and converted into a bluish-black, dry mass, which is cast off, the mortifying process progressing, however, in the depth and laterally, so as to involve the lips, chin and cheeks. Within a few days a considerable portion of the cheeks becomes destroyed and even the bone becomes exposed and necrotic. Rather characteristic is the perforation of a cheek which may ensue within a few days. Externally, in the pale, swollen cheeks, a bluish-black hard spot with a reddish zone of demarcation appears, or with this, there may be associated a large bleb. After the gangrenous area is cast off, the perforation or hole is left leading into the cavity of the mouth (Fig. 45).

The disease seems to affect poorly nourished children, often in the course of an infectious disease, such as measles, scarlet or typhoid. As a rule, fever, cerebral symptoms of loss of consciousness accompany the malady which is fatal within two or three weeks.

The etiology does not seem to be the same in all cases. Schimmelbusch¹ and Babes² isolated a special type of bacillus. Perthes found a streptothrix.

¹ Deut. med. Wchnschr., 1889.

² La Romaine Med., 1894.

Others, such as Buday¹ believe that a spirillum and a fusiform bacillus growing in symbiosis are responsible for the affection.

Rods and spindel shaped elements were found by Perthes² and regarded as variant developmental forms of a streptothrix (cladothrix of Seiffert). Baumgarten takes exception to the theory of bacterial causation, believing the organism found to be secondary invaders. However, the finding of spirillae in the areas of advancing gangrene is believed to be suggestive of a bacterial influence. Bernheim and Popsischill³ found fusiform bacilli



FIG. 45.—Defect in cheek produced in noma. (*Lexer.*)

and spirochetæ, but in the depth a mere plump rod. This latter is regarded as the true exciting organism. Hoffmann and Küster⁴ also identified a bacillus as the causative agent.

The peculiar sharp delimitation and separation of the pulpy putrid tissue has been interpreted as indicating some nerve derangement. Latterly, however, the dominant view seems to be that noma is a form of putrid infection with gangrene as a prominent feature. Being frequently one of the complications of other diseases, measles, typhus, diphtheria, dysentery, mercurial stomatitis, syphilis, etc., it is still a mooted question as to whether it is a reactionary sequel of other infections, or of unique causation.

In view of the varied results of bacterial studies, it is quite comprehensible that noma cannot as yet be considered an entity as far as etiology is concerned.

Treatment.—This consists in the destruction of the gangrenous areas with the Pacquelin cautery, frequent irrigations of the mouth, prevention of aspiration pneumonia, and, according to some authors, the extirpation of the affected area with the knife. As prophylactic measures, the mouths of all children suffering from severe debilitating illnesses should be kept scrupulously clean, all ulcers should be cauterized, and carious teeth carefully attended to.

¹ Beitr. z. path. Anat., 1905, XXXVIII.

² Perthes, München. med. Wchnschr., 1902.

³ Bernheim and Popsischill, Jahrb. f. Kinderh., 1898, XLVI.

⁴ Hoffmann and Küster, München. med. Wchnschr., 1904, 43.

CHAPTER XXXIV

MICROBIC GANGRENE (CONTINUED)

GAS GANGRENE

Emphysematous Gangrene (*microbic or traumatic spreading gangrene, gangrene foudroyante*) produced by rapidly spreading infection of the subcutaneous tissues is a clinical symptom-complex produced by a number of different virulent gas-producing organisms. Much confusion has arisen regarding the nomenclature and etiology, authors, however, being generally agreed regarding the intensity of the infection, its virulence, the production of gangrene and the presence of gas in the tissues. It has been variously termed, traumatic emphysema, gas phlegmon, acute microbic gangrene, fulminating gangrene, gangrenous cellulitis, malignant edema, anaërobic gangrene.

Numerous appellatives have been employed, most of which have merely historical interest. The French authors describe it as bronze erysipelas, a *gangrène foudroyante*. If the gas bacillus or the bacillus of malignant edema alone were responsible, the terms, malignant edema or malignant emphysema would be apt. However, numerous other organisms are known as causative agents. *Gas edema* as been suggested by Aschoff. Other names are *gas inflammation* and *phlegmon*, or *gas gangrene*. The last of these has found wide acceptance, even though the pathological process does not attain the state of tissue mortification, and is more correctly a gas phlegmon. The multiplicity of names is partly due to the diversity of the infecting organisms and the consequent variations in the objective phenomena.

The Bacteriologic Etiology.—Although the gas bacillus (*B. aerogenes capsulatus*) of Welch (and Nuttall) or of Fränkel and the bacillus of malignant edema were formerly regarded as the sole causative agents, more recent researches have shown that a number of other obligate anaerobic bacilli can be cultivated. The bacteria can be described in two groups; (*A*) the non-putrefactive, and (*B*) the putrefactive form.

A. The Non-putrefactive Type.—1. *The Welch or Fränkel gas bacillus* (*bacillus phlegmones emphysematosæ*).

Morphology.—The Welch or Fränkel gas bacillus (described by French authors as *Bac. perfringens*) is found in the earth, dust, soiled uniforms of soldiers, trenches and in the intestines. It is a short plump bacillus with square end, immobile, without flagellae. It is absolutely Gram positive, and can be demonstrated to possess a capsule (Buerger method). Spores can be but rarely demonstrated.

It is easily cultivated according to the usual anaerobic methods. It can be most easily recognized and cultivated by animal inoculation with the employment either of a rabbit in whose ear vein a culture is injected intravenously, or by subcutaneous injection into a guinea pig. In these animals, if they be killed shortly after inoculation, and placed into the incubator, intensive gas production can be demonstrated.

Toxins and Antitoxin Formation.—The question as to the production of toxins is still a mooted one. Certain authors have found that sterilized cultures are not virulent for guinea pigs. Passini, however, claims to have found toxic substances in the cultures of gas bacilli that are lethal for the animal. Klose reports the isolation of a toxin in cultures, which produces hemorrhages and local necrosis in guinea pigs; and, when injected intraperitoneally, causes dyspnoea, fever and death. Intravenous injecotin was

followed by spasm and rapid exitus, the liver and spleen showing hemorrhages and marked anemia.

By the appropriate treatment of dogs and rabbits, this author was able to produce an antitoxin with which he could protect guinea pigs against a lethal dose of the organism.

2. *The Bacillus of Malignant Edema.*

Morphology.—Several types of bacillus of malignant edema have been described; a Gram negative type with flagellae, and highly pathogenic for rabbits and goats. These animals succumb in a very short time with severe symptoms of malignant edema. In stab, gelatin cultures, a cylindrical or bell-like fluid liquifaction takes place.

A Gram positive type has been recognized. This is pathogenic for guinea pigs, the animals dying within 24 hrs. with marked edema. Rabbits, however, are non-sensitive to this type, except for slight local edema that rapidly disappears.

A third type is also Gram positive, is also pathogenic for rabbits and guinea pigs and is said to be identical with Aschoff's gas edema bacillus.

Pfeiffer and Bessau¹ distinguish between the *bacillus of malignant edema* which is unable to produce putrefaction, and similar bacilli of the putrefactive type, and which can produce edema, although considerably less malignant than the true bacillus of malignant edema. The latter bacillus is longer and more slender than the Fränkel-Welch bacillus, its ends more slender and may grow in long forms. It has motility by reason of numerous flagellae. It is variable to the Gram stain and frequently the majority of the bacilli are negative to Gram. The spores are oval, usually central, in no way causing bulging of the bacillus.

In guinea pigs subcutaneous inoculation with the bacillus of malignant edema, a characteristic bloody exudate is produced without or with very slight gas production. Exitus takes place early, and the bacilli can be cultivated after death both locally and in the internal organs and blood. Intravenous injection in rabbits is so toxic that death occurs within a period insufficient to warrant the expectation of multiplication of the bacilli. The toxic effect of the cultures seems adequate to cause death.

Toxin Production.—Ficker² and Silberstein³ were able to isolate toxins and the latter author by the elaboration of a goat serum could neutralize the effect of a lethal dose in guinea pigs.

3. *The Aschoff Gas Edema Bacillus.*

This author was able to isolate (1915–1916) a plump motile anaerobic bacillus appearing in diplobacillus or chain forms, usually Gram positive, but occasionally negative. Spores were noted in a central or terminal situation. In milk, gas formation and coagulation take place. It is distinguished from the Fränkel-Welch bacillus through its motility. It differs from the Ghon-Sachs bacillus being more virulent for rabbits.

B. Putrefactive Organisms.—1. *The Pfeiffer-Bessau bacillus.* This organism has been called the watch-hand (*Uhrzeigerbazillus*), has constant characteristics, more probably identical with the bacillus putrificus (Bienstock). These are short Gram positive rods with rounded ends and marked motility. Their spore formation is active, so that most of the bacilli contain large mobile spores. These are usually terminal and cause an intumescence in the body of the bacillus. They are but slightly pathogenic. Subcutaneous injection in guinea pigs produces local inflammatory infiltration; intravenous injection into rabbits is harmless.

2. *The Pfeiffer-Bessau Paroedema Bacillus.*—This organism has morphologic similarities with the bacillus of malignant edema, but differs from it in its putrefactive powers. This is not a single group, but its members show considerable variation.

The paroedema bacillus varies in size resembling that of malignant edema, poorly motile or non-motile; some Gram positive, others Gram negative. The spores do not alter the width of the organism and are usually central. They are but slightly pathogenic. This type includes a group of organisms not absolutely similar.

3. *The von Hibler Bacillus.*⁴—This is a motile rod and usually a diplobacillus. The spores are frequent and dilate the bacillus. It is Gram positive, but not as strongly as the Welch bacillus. It is pathogenic for guinea pigs, white mice, rats, rabbits, etc. Except for the observations of von Hibler, there are only those of Chiari regarding the occurrence of this in gas phlegmon of human beings.

¹ Pfeiffer and Bessau, Deutsch. med. Wchnschr., 1917, p. 1217, 1255, 1281.

² Ficker, Med. Klin., 1917, No. 45, 118.

³ Silberstein, Wien. klin. Wchnschr., 1917, No. 52, 1672.

⁴ von Hibler, Zentralbl. f. Bakteriologie, Parasitenk. u. Infektionskr., 25, 513, 1899 also Untersuchungen u. d. path. Anaeroben, Fischer, Jena, 1908.

4. *The Ghon-Sachs Bacillus*.¹—This is a strong anaerobic pleo-polymorphous coccoid bacillary organism sometimes, shred-like, or fusiform. In some of the preparations bifurcations have been noticed. It is motile and has lateral flagellæ. Spores may be central or terminal. The bacilli are Gram labile, the young forms Gram positive, the older ones but weakly so. There is no capsule.

Guinea pigs are killed by 0.5 cc. of a 48 hr. sugar culture, death being preceded by gas formation, edema and hemorrhage. Intravenous injection into rabbits produces death with extensive edema.

Toxins have been produced by Ghon and Sachs. The Welch experiment of intravenous injection into animals results positive for gas formation when the animal is kept in the incubator after death.

Anaerobic Bacilli.—Organisms have been found in gas gangrene, whose causal relationship to the lesions has not been established. Of these, there are the Novy² bacillus and the Conradi-Bieling³ bacillus.

The former is an aerobic, motile Gram positive bacillus without spores, characterized by the presence of long and fixed forms, but slight motility, absence of spores, poor growth on agar and strong pathogenic action on experimental animals.

The Conradi-Bieling bacillus resembles those described by Aschoff. The vegetative form is a non-motile, Gram positive thick rod, producing marked gas formation, in carbohydrate media, and liquefaction of proteid media, very pathogenic for guinea pigs that die of hemorrhagic edema and gas formation, whilst rabbits are non-sensitive.

Relationship of the Various Bacteria.—The most dangerous of the bacilli that produce gas gangrene are the Fränkel-Welch and the bacillus of malignant edema, neither being putrefactive types.

The organism found in gas gangrene has been detected in the earth and in the intestinal tract. This explains their easy entry into wounds, particularly during war. The Fränkel-Welch bacillus is the most common of the organisms found.

Next in frequency is the bacillus of malignant edema as a causative agent in an aerobic wound infection.

Clinical gas gangrene, it is true, is most frequently due to the Welch or edema bacillus, but anaerobic mixed infection is common. Thus, the tetanus bacillus is not infrequently admixed in such infections.

Furthermore, anaerobic bacilli may be associated with aerobic organisms, namely, with streptococci, staphylococci, bacillus coli, bacillus pyocyaneus, proteus and others. The streptococcus is particularly important, indeed, may be so preponderating so as to appear to be the gas producing organism.

Some authors believe that certain of the gas producing organisms may be changed into other types. Thus such mutation is said by Aschoff to occur, also by Conradi and Bieling, when a vegetative form of gas bacillus is without spores and flagellæ and is grown upon proteid media. A conversion into a flagellated, spore-bearing form results. Other authors, such as Fränkel, desire to controvert this assumption, suggesting that such observations were due to the presence of a mixed infection.

Pathological Anatomy.—The most important lesions in gas gangrene are those occurring in the musculature, the alterations in the other tissues being secondary. The muscle becomes pale red, dry and filled with small, glittering, silver-like gas bubbles. Later, it takes on a brownish or blackish tone with greenish tint and the gas bubbles enlarge. Then fluidification of the muscle into a blackish, brown, pasty substance with large gas bubbles occurs. At a distance from the primary focus, the muscle undergoes areas of waxy necrosis, becomes greyish-yellow and like fish meat. Associated are small hemorrhages giving the muscles a variegated appearance. The inter-muscular connective and subcutaneous tissues are at first infiltrated with a brownish yellow edematous fluid, that is striking because of its large amount.

Microscopic examination also reveals characteristic changes particularly in the muscle tissues. The gas bacilli are present in large numbers, accumu-

¹ Ghon-Sachs, Zentralbl. f. Bakteriöl., 34, No. 4-7, 1903; also 35, No. 6, 1904; also 36, No. 2, 1904.

² Novy, Ztschr. f. Hyg., 17, 1894.

³ Conradi-Bieling, Feldärztl. Beil., München. med. Wchnschr., 1916, 133 (49), 1023 (455), 1561 (705); also Berl. klin. Wchnschr., 1917, No. 19, 449.

lating in the connective tissue and fatty septa, extending to the subcutaneous tissue and diminishing in number towards the skin itself. In the lumina of the veins, occasional gas bacilli will be found, but not in the arteries.

Microscopically, therefore, the situation of the bacilli corresponds to the assumption that the lesion is primarily one of the muscle. However, to be exact the bacilli actually lie first, in the perimuscular or perifascicular connective tissue and in the lymph spaces. By virtue of the activity of the bacteria the muscle fibers undergo fluidification with gas formation, there being an *absence of any inflammatory and cellular reaction*. Rounded spaces about the muscle fibers represent the gas bubbles. *Pari passu* with gas formation there is a continuation of the degenerative condition of the muscle. The fibers of the latter become fragmented, degenerate into hyaline bodies and into minute particles. All of these detached and separated pieces of muscle element become fluidified into a structureless mass, in which no recognizable histological elements are then to be found. The absence of inflammatory reaction is characteristic for pure gas bacillus action, for leukocytic infiltrations usually indicate mixed infections with cocci. In addition, there is marked edema of all of the tissues.

The three stages in the development of the destructive lesions are recognized by certain authors.

First.—A primary focus develops characterized by the entrance of a foreign body (piece of clothing or shot) in a bullet tract; in it there is more or less gas formation in the subcutaneous tissue and musculature. In this zone there are numerous bacilli with spores and also free spores.

Second.—Adjacent to this and varying in width there is a zone of strong hemolytic edema of the subcutaneous tissue with gas bubbles, containing bacilli without spores.

Third.—A third zone without bacilli but with toxic yellow edematous fluid infiltrating the tissues.

Gas Formation in the Internal Organs.—Welch and Nuttall¹ called attention to gas formation in organs due to the action of the bacillus aerogenes capsulatus. Although the occurrence of gas formation in the organs was at first demonstrated postmortem in experimental animals, Welch believes that such gas formation can occur during life. Other authors take exception to this view.

The more recent observation during the war period would concede the possibility of antemortem changes of this nature, with, however, the reservation that such occurrence precede the lethal outcome by but a short time.

The Blood Vessels.—In cases of gangrene due to infectious processes, it has always been a mooted question as to whether the vascular lesion or direct bacterial action is responsible for the gangrene.

In gas phlegmon blood vessel lesions have been regularly encountered. Some authors have described a fatty degeneration of the vessels and a proliferating endarteritis with gas gangrene. Legros describes also an obliterating endophlebitis. Inasmuch as the entry of the bacteria into the blood vessels has not been demonstrated, it is believed that the lymphatics are invaded and possibly the capillaries, the latter portal of entry explaining the bacteriemia.

Bacteria, however, have been shown to enter the vein walls, in gas gangrene when the bacilli of malignant edema are associated.

Period of Incubation.—Since the gas bacillus can vegetate in the wound for some time, the period of incubation varies. As a rule, manifestations appear within the first four days.

¹ Welch and Nuttall, Bull. of the Johns Hopkins Hosp., 1892, 3, 81.

According to Hancken¹ the gas phlegmon appears on the first day in 21 per cent; on the second day in 33 per cent; on the third day in 15 per cent; on the fourth to the sixth day in 4 per cent; on the seventh to the eighth day in 3 per cent, and from the eleventh to the twentieth day in 1 per cent of the cases. Of 119 cases studied by Franz² gas formation was noted 29 times within the first two days; 18 times after three days, 14 times after four days.

Occasionally there is a very short period of incubation no longer than a few days after injury. It is said by certain authors that infection may be carried through field hospitals, through kitchen utensils, dishes and instruments. This is doubted by others. For it is known that war wounds often harbor anaerobic organisms that remain dormant for weeks or months, and then by reason of subsequent tissue injury light up and become activated.

Latent Infection with Anaerobes.—It is believed (Melchior) that organisms of this type may be buried for a long time even in healed wounds and become active after weeks or months. This has been shown to be the case with the tetanus bacillus,³ when buried bullets or shot fragments are removed from old scars and the symptoms of tetanus develop. The spores of the tetanus bacillus are said to remain for a long time in the scar and are activated and made virulent through the trauma of operation. Similarly, gas bacilli can be reactivated. Indeed Wieting⁴ reports a gas phlegmon following grenade wound with healing. Six months later, after an attempt to remove the imbedded metal, gas infection occurred with a lethal outcome. Enough cases in which the primary wounds had already healed with good cicatrization have been described to confirm the correctness of such observations (Melchior,⁵ Küttner,⁶ Hodesmann⁷).

Pathogenesis of Gas Gangrene.—It has been said that the majority of all war wounds contains anaerobes. Bacteriologists working in the neighborhood of the battle fields have found gas bacilli in a large percentage of wounds during the Great War, though no clinical manifestations were present. Even in ordinary infected wounds gas bubbles were not infrequently seen, so that from the practical standpoint it must be accepted that almost all of the wounds contain gas bacilli. This does not signify however, that all wounds become gas phlegmons, inasmuch as special factors must be present to facilitate the activity and develop the virulence of the anaerobes.

Two additional factors, namely, earth infection and special wound conditions are necessary. Entrance of earth carries with it anaerobes that have been derived from the excreta of animals. Such earth is carried there by hand grenades, fragments or even when pieces of clothing are carried in by bullet shots.

The bad wound conditions referred to include laceration, contusion, extensive compression and detachment of tissue fragments with tearing of vessels and circulatory insufficiency of the wound. Anaerobic organisms develop rapidly in the necrotic tissue. The leucocytic poisons elaborated and the negative chemotactic reaction induced by the organisms explain the absence of the usual cellular exudate.

The Incidence of Gas Gangrene.—Amongst the wounded in the late war, gas symptoms are said to have occurred in the following frequency. Wieting 3–5 per cent, Marwedel⁸ 2.8 per cent, Rumpel⁹ 3 per cent and Franz¹⁰

¹ Hancken, *Feldärztl. Beil. z. München. med. Wchnschr.*, 1916, 1030 (462).

² Franz, *Deutsch. med. Woch.*, 1917, 39, 1220; also *Bruns Beitr. z. klin. Chir.*, 1917, 106, 443; also *Deutsch. med. Wchnschr.*, 1917, 14, p. 446.

³ Buerger and Heimann, *Am. Jour. Med. Sc.*, Aug. 19, 1905.

⁴ Wieting, *Deutsch. Ztschr. f. Chir.*, 1917, 141, 1.

⁵ Melchior, *Berl. klin. Wchnschr.*, 1915, 5, 97.

⁶ Küttner, *Bruns' Beitr.* 103, 300, 1916.

⁷ Hodesmann, *Deutsch. med. Wchnschr.* 1917, 22, 687.

⁸ Marwedel, *Feldärztl. Beil. z. München. med. Wchnschr.*, 1915, 30, 1023, 479.

⁹ Rumpel, *Samml. klin. Vortr.*, 1917, 736, 39, 329.

¹⁰ Franz, *Bruns' Beitr. z. klin. Chir.*, 1917, 106, 443.

2 per cent. Where hand to hand battles occur gas bacillus cases are frequent; also where resuscitation facilities are poor and wounds are neglected. During the wet period with considerable rainfall, cases are more frequent than in dry periods, probably due to the wetting of the clothes and accumulation of anaerobic organisms in clothing already soiled with earth.

It was by far more prevalent while fighting took place on the well fertilized fields of Belgium and France, than in the mountainous regions of the Italian and neglected forests of the Russian fronts.

Localization of Gas Gangrene.—In view of what has been said, gas gangrene must be expected in those portions of the body where muscle tissue is present, particularly where large muscle masses occur, namely, in the extremities. Thus, the lower extremity is more frequently affected than the upper ($2\frac{1}{2}$ times). It occurs in the trunk, where there are large muscle planes; but rarely is it found in the region of the head and neck, infrequently affecting the foot and hand. It may be multiple, implicating more than one extremity.

The cases in which gas phlegmon of the brain occurred are not due to the organisms described here, and doubtlessly are the result of extension from head wounds containing anaerobes. Gas gangrene of bones does not occur, nor of the abdominal organs. Reports of authoritative cases of gas infection of the liver have not been forthcoming, and the spongy liver reported at some autopsies (Schaumleber) must be regarded rather as a postmortem process.

Types of Gas Gangrene Infection.—Epifascial gas phlegmon of more benign nature has been differentiated from the malignant subfascial form (Payr¹). The former usually heals after multiple incisions; the latter is fulminating, converting the muscle into a pasty mass; the extremities die off and require amputation or exarticulation to save life. The deep form of infection corresponds to the gas gangrene and gas phlegmon of other authors and is well accepted. The superficial form is regarded as a less virulent type of infection, and is thus described.

The Superficial Form.—Its seat is between the skin and fascia, the muscle being uninvolved. The skin is edematous and shows deep orange or almost coffee colored patches. The subcutaneous tissue is infiltrated with amber colored fluid; the skin may show blebs; and subcutaneous crepitation due to gas can be elicited. The fascia is not necrotic, but the underlying muscle seems to be healthy. The general systemic condition shows marked disturbance, with fever and rapid pulse; but the prognosis is good. Some authors (Bier²) refuse to accept this type as being one of true gas phlegmon, believing that the epifascial form of Payr is also a muscle disease due to infection of a bullet wound and represents an extension of a deep focus, one of such slight virulence as to give the above described manifestations. It is noteworthy that true gas phlegmon does not occur after bullet wounds that fail to implicate the musculature.

In short, according to some the *epifascial form* may be regarded as a mild distribution of this infectious process in superficial planes, and arising from a primary deeper focus. It differs from the true gas bacillus infection, in that it usually yields promptly to conservative treatment with multiple incisions.

Summarizing the types of gas infection we may speak of the following:

First, *local gas phlegmon* which is benign and has no tendency toward unlimited extension, but localizes itself involving single muscles.

¹ Payr, München. med. Wchnschr., 1915, 57; also Med. Klin., 1916, 442.

² Bier, Med. Klin., 1916, 14, 355.

Second, *progressive gas phlegmon* which is malignant, in that muscle disintegration may extend over the whole of a portion of the body (member) and usually ends in gangrene; and

Third, *anaerobic sepsis* which extends rapidly without bounds, is attended with severe general symptoms, and terminates fatally.

A. The Toxins of Gas Gangrene.—The general symptoms correspond well to the clinical picture of a severe poisoning, the toxins being partly of bacterial, partly of tissue origin. The question of the development of a true toxin from the gas producing organism is a mooted one as regards the Fränkel-Welch bacillus. However, in the case of the bacillus of malignant edema, true toxins have been demonstrated (Ficker¹), the intravenous injection of very small quantities of which, produces a lethal effect in rabbits. This finding would lead to the expectation of appropriate serological treatment.

According to Wassermann² all gas bacilli produce a similar poison, just as staphylococci produce a staphylolysin, so that this author believes that the poison is derived rather from degeneration of the bacterial bodies, than from products of their action.

Clinically, however, there seems to be evidence in favor of the elaboration of a bacteriogenic blood poison. Indeed, one that attacks the hemoglobin of the blood. The Fränkel-Welch bacillus, also the Aschoff, have a lytic effect on the red blood cells. Other authors (Kamen³) speak of a toxin with a specific action against the leukocytes (leukocidin), in addition to the active, negative chemotactic action of the poison. The most injurious effect of the bacillary poison is the chemical action on the hemoglobin, which is liberated from the red blood cells, and converted into methaemoglobin. Hemoglobin, therefore, appears in the blood serum and in the urine. Clinically, this action has been observed in puerperal processes, and an attempt made to correlate the brownish, cyanotic skin color, air-hunger, and a brown blackish appearance of the urine, with the production of the hemoglobinaemia and the hemoglobinuria. Such severe disturbances in the blood, however, have not been observed in gangrenous processes, but rather in the puerperal. Enough data has been forthcoming to confirm the theory of the existence of a toxin. The yellowish and brownish spots of the skin have been regarded as due to hemolysis, and the marked icterus in the lethal cases, as due to the rapid degeneration of blood cells.

The histogenic poisons developed locally have not been thoroughly studied. It has been shown that autolysis of tissues produces a poison, and here the muscle tissue in its degeneration might be considered as the origin of a toxin. The symptom of marked collapse has been due to anaphylactic shock. As the muscle protein breaks down through the peptonizing action of the bacilli, toxalbuminates or foreign body proteins are absorbed, cause hypersensitization and anaphylactic symptoms. Furthermore, acids—carbonic, lactic, butyric, propionic, etc.—as they are formed in the process, are said to irritate the respiratory centers, and produce Kussmaul's type of breathing.

General Symptoms.—In the severe cases of gas gangrene the general symptoms are marked, collapse being an early sign of a rapidly progressing gas gangrene. The face has peculiar pale appearance, whilst the tongue remains moist. The pulse becomes very rapid, so that a frequency of 140–160 is not unusual. The blood pressure sinks rapidly, the lips become cyanotic. Striking changes in respiration are noted, often of the Kussmaul type, similar to that of diabetic coma. Dyspnoea with the employment of all the accessory respiratory muscles is characteristic, due to central irritation of the respiratory center. This manifestation has been explained on the assumption that acids elaborated in the gangrenous process are absorbed, or that bacteria produce carbonic acid in the blood itself (Pribram) that acts directly upon the respiratory center.

The temperature is not usually high, may be normal or subnormal, and it is only when there is slow development of gangrene that there is elevation.

Icterus is a dangerous and grave manifestation, an indication of anaerobic sepsis, and that the hemolytic process is making itself manifest in the circulation. The assumption that liver changes are responsible does not seem

¹ Ficker, Med. Klin., 1917, 45, 1181.

² Wassermann, Med. Klin., 1916, 17.

³ Kamen, Zentralbl. f. Bakteriologie, Parasitenk. u. Infektionskr., 1904, 35, 554–686.

tenable, in view of what has been previously said regarding liver lesions. Vomiting and singultus are often associated with the icterus. Marked hyperhidrosis is striking.

The *blood picture* very soon becomes altered, the hemoglobin being diminished, and the erythrocytes showing the picture of anemia with marked anisocytosis (macro- and microcytes). The white blood cells show changes, there being eosinophilia and leukopenia. The absence of increase in the number of neutrophils is said to be characteristic for gas gangrene. The blood picture persists even after convalescence for a considerable period of time, with a marked anæmia, poikilocytes, polychromasia and megalocytes.

There is diminished coagulability of the blood. The urine contains albumin, granular casts, often blood.

All of these symptoms may be present with complete conservation of consciousness. Often euphoria is noted, and the picture is not unlike that of poisoning by serpent venom, and sometimes of pancreas necrosis, all being manifestations of severe intoxication.

Local Symptoms. *The Wound.*—Where the wound is wide open, the musculature becomes dark, blackish and crepitates, and the uninvolved muscles are glassy by reason of extensive infiltration with edematous fluid. Gas bubbles glitter here and there like pearls in the tissue. The skin edges become necrotic. The absence of inflammatory reddening and heat is characteristic. When it is present, it is due to mixed infection. The fluid of the pure cases of gas bacillus infection is serous or resembles laked blood filled with bubbles of gas. Swelling and pain are always present, the result of collateral edema. The regional glands are not enlarged.

The Skin.—Where the process is developed in the depth, the skin is at first but little involved. Often, over the muscle focus, the integument has a white, glistening, swollen appearance, in which the dilated veins are prominent. When the gas formation approaches the skin, characteristic changes appear, namely, a brownish or orange colored patch, or bluish or violet areas of discoloration. With the former there may be blebs with watery or yellowish fluid, that are distributed in geographic figures or discrete fashion. In the region of the brownish spots, the skin may undergo a leather-like necrosis, and an incision into it evokes no bleeding. Where the bluish discoloration is present, the gangrene is more intensive, the skin dies off rapidly together with large parts, or the whole of the extremity. Such blue patches are always the precursors of total necrosis and gangrene involving all the layers. The brownish patches indicate more limited necrosis often only of the skin. When patches of skin are sequestered, secondary infection with suppuration may take place.

The Gas Formation.—This is the most characteristic symptom, being the product of the breaking down of the muscle carbohydrates and the decomposition of proteins. This accumulation of gas may be so enormous, and its migration so distant that when the lower extremity is involved, gas bubbles are said to have travelled into the subcutaneous tissues of remote parts. The distension may be so great that incision into the skin gives rise to a blowing or puffing sound. Palpation or percussion suffices to detect the presence of gas. X-ray examination shows free gas in the tissues. In the picture, spots or streaks between the muscle and into the subcutaneous tissue can be visualized, in territories far removed from the bullet wound.

The Edema.—Usually marked edema accompanies gas production, and is responsible for the appellation "gas edema." The places vary, according to reports, some having marked gas production without gas edema, others marked edema without gas. The edema of gas gangrene is rather characteristic. It

is of yellowish color or serous, causing marked bulging of the subcutaneous tissue, and muscular interstices and vascular sheaths. This is very striking about the sciatic nerve. The edema can become brownish due to blood admixture. Two views as to the significance and purpose of the edema have been suggested. According to one it is defensive and tends to combine and nullify the action of the toxins and lytic products. According to other views the edema has a contrary function, namely, in that it contains *aggressins* which are toxic for the cells of the body. As such it would assist the bacterial action as an advance guard.

The Gangrene.—This should be described under the classification of infectious gangrene, being the direct clinical expression of the action of certain bacteria. Gas gangrene, occurs directly in the infected wound, and not at the termination of an extremity. In this way it differs from the gangrene that results from injury of important vessels. The necrosis begins in the muscle. The action of the bacilli and the development of gas produce a pale red discoloration of the muscle which gives way to a darker color. Finally, as fluidification takes place, a chocolate porridge-like mass is formed. All the individual muscles are not equally affected, so that on cross-section, at amputation, or autopsy, the mottling with the contrasted involved and non-involved groups is striking.

From here the gangrene extends into the external skin which becomes bluish or violet in color, and then grayish black. The epidermis is lifted off with the formation of bloody blebs, and the process extends more rapidly peripherally than centrally.

When the gas necrosis surrounds the limb so as to involve all the circulatory channels, the peripheral parts show evidences of impaired circulation, in absence of pulse, anemia, and coldness. In this way a secondary anaemic gangrene of the peripheral portions of the extremities may result because of poor nourishment. These two processes, therefore, may meet and become confluent, one descending, the other ascending.

The process of mortification may be so rapid as to implicate a whole limb within a very few hours, and is due to the enormous rapidity of the multiplication of the organism. Thrombosis of the large veins may add to the rapidity of the mortifying process. Some authors attribute the fulminating form of gangrene to the contractile effects of the toxins on the vessels; others, to the accumulation of products that cause necrosis by pressure.

Vessel Injury and Gas Gangrene.—When large vessels of an extremity are injured by bullet wound, or when it becomes necessary to ligate large vessels such as the popliteal because of hemorrhage, the liability to gas gangrene infection is already present and the progress of such infection is greatly enhanced. Thus, after ligation of the popliteal during the Great War, it was observed that gas infection developed frequently, necessitating amputation. Of 39 cases studied by Bier and Specht¹ in which amputation for gas gangrene was necessary, there were 33 in which injuries to the large arteries had occurred. According to some authors, however, the gas formation is a secondary process, consequent upon the arterial thrombosis, when anaerobic, saprophytic organisms multiply in the dead tissue.

Clinically, however, it is difficult to differentiate the two types, and it must be accepted that circulatory disturbances are an important factor in predisposing to anaerobic infection.

Diagnosis.—In severe cases the diagnosis is easy. The so-called anaerobic sepsis is characterized by the altered breathing, the deep collapse, the weak pulse, with conservation of consciousness. The progressive gas phlegmon with its edema, emphysema, foul odor, discoloration of the skin, the gangrenous change of the muscle tissue, the peculiar pallor of the face

¹ Bier and Specht, Bruns' Beitr. z. klin. Chir., 1916, 101, 271.

with the poor general condition—all these are characteristic manifestations. Severe pain often initiates the onset of the process, and when it occurs, a few hours or a day after the injury, is a premonitory sign of significance. When in doubt, an incision is indicated which may bring to light the peculiar change in the muscle, or possibly even gas. Severe streptococcus phlegmon may also produce gangrene of the extremity, but gas is not present, nor is there a characteristic sound on percussion.

Morbidity and Mortality.—Early in 1918, Gross¹ had 2,796 wounded men pass through his hands, of whom 101 (3.6 per cent) developed gas gangrene. Late in 1916 he treated 1,676 wounded men,² 33 of whom (1.9 per cent) developed gas gangrene. In October, 1918, Sieur and Mercier³ reported that fewer than 0.5 per cent of the wounded developed gas gangrene in the advanced and intermediate zone. This was undoubtedly due to improved hygienic conditions and character of the soil (non-fertilized). Lardennois⁴ in 1916 reported 500 cases of gas bacillus infection with 15 per cent mortality; and Ivens⁵ in 1917, 460 cases with 9.5 per cent mortality.

Regarding definite gas gangrene as distinguished from gas bacillus infection in general, Gross, in 1916, listed 101 cases with 56.5 per cent mortality, while Ivens, in 1917, reported 107 cases with a mortality of 26.4 per cent. It must be emphasized here, however, that of the cases reported by Gross, those which were treated within twelve hours after the wound was received had a mortality of only 10.9 per cent. This indicates more clearly than any description could, the importance of early treatment.

Treatment.—The general principles include the following: detoxication by serum; control of shock; the intravenous injection of sodium bicarbonate for acidosis; the early and thorough removal of all injured tissues, infectious agents and foreign bodies by surgical intervention, although it is not always necessary to remove large areas of skin and subcutaneous tissue. All suturing is to be avoided; free drainage is to be instituted; the proper splints applied; and Carrel-Dakin solution used. The question of amputation depends on the condition of the patient, the extent of infection, its proximity to the body and whether or not the infection can be controlled by conservative measures.

For the collapse symptoms hypodermic stimulants, hypodermoclysis, intravenous injection of glucose solution (5 per cent), subcutaneous injections of adrenalin and salt solution are indicated. In view of the hypothetical assumption that the systemic manifestations represent the effects of acid intoxication, subcutaneous soda solution ($\frac{1}{2}$ per cent) and intravenous administration have been followed by definite results. Hypertonic solution of salt intravenously injected is also recommended (Hercher, introducing sodium chlorid 8.5, potassium chlorid 0.3, calcium chlorid 0.3 with water up to 100).

Van Beuren gives the following general rules used for treatment of gas bacillus infection during our recent war. First, operate as early as possible. Second, use nitrous oxid-oxygen anesthesia if possible. Third, prepare the part with the minimum amount of delay and trauma. Fourth, avoid tourniquets. Fifth, make incisions longitudinally and half again as long as you think they need be, both in the skin and fascia. Sixth, leave as much skin as you dare in your débridement. Seventh, go between, rather than through, normal muscles, and do not cut across them unless you have to (better a long separation between two than a short cut across one). Eighth, however open the wound as thoroughly and freely as you possibly can. Ninth, excise all torn, crushed, discolored, noncontractile muscle, until you have left only that which is firm, of normal color, actively contractile, and which bleeds readily. Tenth, make a careful and conscientious search for and remove all loose bone and foreign bodies, especially clothing and blood clots. Eleventh, stop the

¹ Gross, G.-Bull. de l'Acad. de med., Dec. 26, 1916, 76, 586.

² Gross, G.-Bull. et mém. Soc. de chir. de Par., 1917, 43, 636.

³ Sieur and Mercier, Bull. de l'Acad. de méd., Oct. 29, 1918, 80, 394.

⁴ Lardennois and Baumel, Presse méd., Nov. 16, 1916, 24, 506.

⁵ Ivens, Med. Press & Circular, 1917, 103, 12.

bleeding; leave the wound wide open and separate its walls with wet gauze, laid in, not packed in. Twelfth, use Carrel-Dakin tubes, if you know they will be properly cared for, otherwise omit them. Thirteenth, use plenty of dressings and make careful splint fixation of the part. Fourteenth, do it all as rapidly as you possibly can.

We may divide the treatment into surgical treatment, treatment by hyperemia, by oxygen insufflation, medical treatment, transfusion of blood, and serum therapy.

Surgical Treatment.—In the mild cases of local gas phlegmon, wide and extensive incision are the most reliable means for establishing a cure. The incisions must be carried well into the healthy tissues, until bleeding muscle is reached. This is to be followed by loose tamponade drainage, the use of Carrel-Dakin solution and splinting, to secure adequate repose of the parts. When we can detect more extensive infiltration of the interstices of the muscle with gas and edema; when the vascular sheaths are involved, and the process is recognized in the discoloration of the skin, and subcutaneous emphysema—the excision must be carried along such planes as seem to be involved, along the vessel sheath and through the skin. The incisions through the skin are best made in multiple fashion.

Where the affection is more virulent, and shows marked progressive tendencies, more radical means are resorted to. So certain authors recommend instead of the longitudinal incision (Fessler¹ and Fründ²) transverse incisions, which enable a more adequate and accurate investigation of the muscle masses to be made. Indeed, in very bad cases, it may be necessary to excise whole muscular territories.

When the gangrenous process threatens to invade the opposing groups of muscles, to encircle the bone and to creep over the joint immediately above, amputation is in order. The well developed gangrene of a portion of a limb is also an indication. Should severe fractures through bullet wound (of the long bones) complicate, amputation is also recommended. Even when the gangrenous process is not as yet in evidence, but when the general symptoms are severe, with rapid and weak pulse, threatening collapse, ablation of the limb must be considered.

It is best to ablate in healthy tissues, at least beyond those macroscopically involved and beyond the edema, although cases have been reported as cured where the amputation was very near and even through diseased parts. In very extensive cases, exarticulation may be necessary. This procedure is not so dangerous when done through the shoulder and gives good operative results. A similar operation through the hip, however, is a dangerous surgical procedure with a high mortality.

Lawson³ believes that the best results can be obtained by treatment of the subcutaneous tissues with nascent oxygen in the form of injections of neutral hydrogen peroxide. Infiltration of the healthy tissues with oxygen above the line of spreading gangrene is sufficient to check the advance of the infection, and in the majority of cases, the limb may be saved. He believes that amputation of the limb for acute emphysematous gangrene is unnecessary, unless all of the tissues are involved over an extensive area, thinking that high amputation may prove fatal from shock.

Treatment with Hyperemia.—This includes active hyperemia and congestive or obstructive (Stauung).

¹ Fessler, *Feldärztl. Beil. z. München. med. Wchnschr.*, 1917, 10, 331.

² Fründ, *Bruns' Beitr.*, 1916, 98, 447.

³ *Birm. Med. Rev.*, 1915, LXXVIII, p. 67.

Obstructive Hyperemia.—Bier recommends the rhythmic method, claiming good results. When the usual method is employed, 22 hours application and 2 hours interruption are not recommended. Although these methods have been well developed on the Continent and particularly in the Central States, they have found but few adherents in America.

Oxygen Insufflation.—Because of the danger of oxygen embolus, this method has not won many supporters. It had been recommended in the form of insufflation into the tissues. Intramuscular injection of 3 per cent hydrogen peroxide has also been suggested with a fatal result (Borscher).

Local Medication.—Various types have been used, such as the washing with peroxide, and Dakin's solution. Charcoal has been used with a view to combine with the aggressins formed by the bacteria. None of the local methods of treatment have had worth-while results.

Blood Transfusion.—Both as a prophylactic measure before amputation or after this procedure, blood transfusion is exceedingly valuable. It is worthy of a trial for its beneficial effects in combatting the toxic results of infection.

Serum Therapy.—For the elaboration of a dependable serum, it is necessary to employ something that not only has an antitoxic function, but also is anti-infectious, in the sense that it can inhibit the enormous multiplication of the organisms in this disease. The existence of both histogenic and bacterial poisons, as a result of the action of the bacteria, makes it hard to find an appropriate serum.

An antibacterial serum was prepared by the firm of Hoechst which is a polyvalent, antibacterial, immune serum procured from horses. In the production of it, the *Fränkel-Welch* group, the *gas edema* group and the *putrificus* group were employed. It was given a trial during the Great War in doses from 20–40 cc. Rumpel injected it locally, just central to the wound; he also tried intravenous application. His results were considered satisfactory in that the mortality was reduced. Anaphylactic symptoms appeared only in a few cases. Aschoff compares a mortality of 43.9 per cent in the cases in which the Hoechst serum was used, against a mortality of 68.7 per cent without any. Weinberg and Seguin employed an antitoxic and bactericidal serum including the following group: *bacillus perfringens* (Fränkel-Welch), *sporogenes*, *oedematicus*, *vibrio septique* and *bacillus hemolyticus* (Weinberg and Seguin).¹

Statistics on the efficacy of anti-gas bacillus serum are somewhat meagre, but are on the whole favorable. Elser advises the following routine for serum treatment.

1. A prophylactic dose of polyvalent serum, given as early as possible after the receipt of the wound, combined with tetanus antitoxin.

2. Bacteriologic examination of the wound and establishment of the presence of gas bacillus infection and determination of the variety of the bacteria. The determination can be made in about 24 hours.

3. Administration of the specific serum, either single or polyvalent or "pooled," according as there are one or more gas formers found and also antistreptococcus serum.

Sacquepee² recommends the following procedure for differentiation to determine the type of anaerobe present.

In each of four test tubes is placed 1 cc. of macerated gangrenous tissue and to three tubes respectively is added 1 cc. of each of the three antiserums. After incubation for half an hour the contents of each tube is injected respectively into one of four guinea pigs. The one protected by the serum shows no reaction. The others die. They usually become sick in from 6 to 12 hours.

The various reports generally agree that intravenous injection (while not always possible) is to be preferred, in combination with deep muscular injection, proximal to, but in the vicinity of the wound.

Dosage: 5–15,000 units of specific or pooled serum intravenously to be repeated in 2 hours if no improvement occurs. At the same time, an equal amount is given intramuscularly in divided doses. This can be repeated in 24 hours, followed by daily injections.

¹ Weinberg and Seguin, *München med. Wchnschr.*, 1917, 152 and 848.

² Sacquepee et de la Vergne, *Bull. de l'Acad. de méd.*, 1919, 506.

Anaphylactic reactions are rare. It is emphasized that sero-therapy is entirely auxiliary, and in no way replaces operative treatment of wounds. The time of application should be as early as possible, since it is practically useless when the infection reaches the stage of septicemia.

Gangrene Due to Pyogenic Bacteria.—The rôle of this type of organism in causing tissue mortification has not been carefully studied so that we can but dwell superficially on this theme. Enough is known, however, to permit of the conclusion that streptococci of various types, and other organisms when virulent, or in symbiosis, are able to cause extensive local tissue disintegration in a direct fashion, or in a secondary or indirect way by virtue of thrombosis induced locally in arteries and veins.

The direct alterations in some of the streptococcal forms are of a destructive type and are quite different from the usual purulent lesions. The skin of the affected region may rapidly take on a yellowish, brownish or bronze color, a significant appearance in these virulent infections.

The secondary gangrene of parts in or distal to the infected area, is often of the dry type when digits are involved and due to a contiguous thrombotic process in larger arteries and veins.

Dry gangrene of one or more phalanges may follow rapidly in the wake of a severe infection of the palmar sheath, with or without infection of the dorsum of the hand. *Streptococcus hemolyticus* is the more common offending agent. Dry gangrene of the fingers or toes may rapidly ensue, and is probably due to thrombosis of the digital vessels at the base of the finger. It is secondary in the sense that it is one of the complicating effects of the infection on the larger source of blood supply. Therefore, it is not a necrosis of tissue due to the direct action of the organisms as is the case with many of the anaerobes. Extensive direct necrosis may here, too, be due to the bacterial influence.

The clinical course, which was well exemplified in one of the author's cases recently observed, may be briefly summarized as follows:

Severe infection apparently located in the palmar sheath of the index finger with lymphangitis extending up to the elbow and above, and temperature of 104° for about one day before the patient was seen by the author. Two small median incisions over the palmar surface of the first and second phalanges liberated turbid fluid from the tendon sheath. Another small incision over the dorsum within the zone of lymphangitis, permitted the same type of fluid to escape. Within twenty-four hours following this incision, the lymphangitis had extended to the axilla, and the following condition of the hand required further operative procedure. The dorsum was evidently the seat of an extensive streptococcus infection, and the palmar infection had spread to about three quarters of an inch farther down into the palm. The two distal phalanges of the fore-finger were bluish black and gave all the signs and had all the appearance of an early stage of gangrene.

Multiple incisions were made over the dorsum of the hand, draining a large amount of purulent fluid that had collected within twenty-four hours, and the palmar incision was carried three quarters of an inch farther down into the palm. By these incisions the infection was controlled, so that no further operative intervention was necessary. However, the two distal phalanges became rapidly mummified.

Here we may assume that the streptococcus infection (*streptococcus hemolyticus* in pure culture) was of such virulence as to cause contiguous thrombosis in the digital arteries, and mortification of the two distal phalanges.

CHAPTER XXXV

GANGRENE COMPLICATING INFECTIOUS DISEASES

Typhoid Fever.—Recent authors (Klose¹) have called attention to the twofold causal elements that occasion vascular symptoms in the course of typhoid fever, namely: The injury to the walls of the peripheral vessel, and a central specific affection of the vasomotor center.

When the larger arteries are involved, thrombosis, hemorrhage and gangrene occur; and the bacilli or their toxins may simply increase the permeability of the capillary endothelium, and bring about edema and transudates.

Hyaline thrombus formation resulting from parietal infectious injury of the vessel wall, with stenosis of the vessels and localized circulatory disturbances are reported. Corresponding to these changes we encounter the complication of typhoid fever, namely, hemorrhages into the various organs.

The larger arteries are described as containing foci of degeneration and inflammation. Involvement of the cerebral arteries is reported in the literature (Jaffe²).

Gangrene of the peripheral parts of the extremity may be the issue. External causes such as cold, and the chemical factors predispose to and increase the severity of the gangrene. Necroses of the feet, fingers and forearm, the genitals and nose have been reported. These were rather common complications in the Great War, when toes were usually found involved, although in certain cases, gangrene extended to the ankle or higher. Sometimes it was symmetrical or multiple. Usually operative intervention became necessary.

A *prodromal stage* is characterized by intense paraesthesiae and pain, and sensory disturbances in the affected extremities. The pain may last for weeks, and may be attended with pallor and a marmorated appearance of the skin before gangrene appears. The latter may attend the early part of the clinical course, or after the temperature has attained the normal.

In infection with the *paratyphus* bacillus, *mycotic aneurysms* may develop. When these are situated in the vessels of the extremities, circulatory disturbances may result. Gangrene of the forearm was barely averted in a case (Sick³) in which a mycotic aneurysm was located at the bifurcation of the brachial artery.

It has been assumed that bacterial emboli entering the vasa vasorum are responsible for the vascular lesions.

Gangrene in Recurrent Fever.—Symmetrical gangrene of the toes is one of the complications of this affection. In some cases circulatory disturbances, pain and cyanosis of the skin may precede the necroses. Perhaps in addition to the action of the spirochætes, external factors such as cold may be contributing causes.

For further consideration of gangrene complicating infectious diseases, the reader is referred to Chap. LXXVI on Acute Arteritis.

¹ Klose, *Ergebn. d. Chir. u. Orth.*, 1921, **13**, p. 74.

² Jaffe, *Med. Klin.*, 1918, nos. 9, 22, 23, 24.

³ Sick, *Munchen. med. Wchnschr.*, 1918, p. 237.

CHAPTER XXXVI

INJURIES TO THE BLOOD VESSELS AND GANGRENE

The traumatic lesions of the blood vessels may be described as including firstly, recent injuries; secondly, pseudo-aneurysms or that type which has been described as pulsating hematomata; and thirdly, well developed aneurysms.

Recent Injuries.—Statistics (Stich) taken from the Great War show wide variations; but in the armies of the Central Powers from 40 to 45 per cent of all injured, suffered vessel lesions. Not more than one-half of those who received bullet wounds of the vessels arrived alive at the hospital stations. Often spontaneous cessation of hemorrhage takes place, especially if of venous origin. Injuries of the veins from bullet wounds are more common than those of the arteries.

A knowledge of vein injuries is important, in that these may lead to remote functional disturbances, even though the immediate effects do not seem to be threatening. Indeed, the functional disturbances that follow may last for years, while the cause thereof may be wholly over-looked.

Even bullet wounds of the arteries may cease to bleed spontaneously. If these facts are taken into consideration, the incidence of vessel injury is in all probability greater than statistics would show.

Bullet wounds of the peripheral arteries most frequently involve the femoral and popliteal; wounds of the axillary and brachial arteries are somewhat less common.

Pathology.—The character of the vascular lesions would depend to a certain extent upon the character of the shot. Large grenade fragments or shrapnel may occasion the severest tears. When the pieces are sharp the vessels may be incised as if with a knife, and abundant bleeding ensue. Tangential trauma may produce contused wounds and holes; or large vascular wounds may result with consequent retraction of the distal and proximal ends of the artery. In the latter instance, bleeding may be but minimal. If infection does not take place, thrombus formation and organization follow. The smaller vessels are usually torn through the action of infantry bullets. In the larger vessels, the same shot causes extensive destruction, not only by direct action, but by the secondary impact and penetration of contiguous or nearby bony splinters. Circular and also slit-like orifices are occasioned, the latter frequently being smaller than the caliber of the bullets.

The blunt forms of traumatism produce three types of injuries; (1) total tearing with complete interruption of the continuity of the vessel; (2) partial rupture with lateral injuries; and (3) rupture of the intima and media with intact adventitia. Such lesions less frequently occur in the veins, but the latter more often are injured in the neighborhood of comminuted fractures.

Injuries Due to Treatment.—Vascular injuries sometimes follow joint dislocations. More important are the observations concerning injuries to vessels in sequence of orthopedic attempts to correct position in old dislocations.

The author recently had occasion to see a young woman in consultation, in whom the femoral artery was torn in an attempt to correct an old ankylosed hip. Five days after the injury, the greater part of the foot was in a state of *gangrene*; all the usual palpable arteries of the extremity failed to beat, and there was an enormous hematoma occupying the

inguino-femoral region, with brawny sanguinous infiltration of a large part of the upper and inner aspects of the thigh. Spontaneous cessation of the hemorrhage had occurred by the pressure hematoma.

As many as 20 such observations are recorded by Körte in dislocated shoulders. Complete tears, as well as lateral holes, have been observed, and in 3 autopsies injuries of the veins are reported. The factors responsible for the ruptures, were the employment of excessive force, abnormal friability of the vessels, adhesions of the vessel sheath with the contiguous bone or joint capsule or simultaneous fracture of the head of the bone (femur or humerus).

Laceration of the blood vessels has been known to follow *severe muscular exertion*. When *brisement forcé* for the treatment of ankyloses of the knee joint, occasioned vessel rupture, gangrene of the extremity was a complication in 9 cases (Salzer¹).

Gangrene of the lower extremities is a complication of severe general body concussion and after burial or entombment under earth following explosive shells that have penetrated into nearby earth. The gangrene has often been attributed to thrombosis of the vessels. In other cases, where the upper extremities were also involved, the cause remained obscure, since the vessels were found patent. Perhaps some of these eventualities are referable to a traumatic vasomotor spasm (Chap. XCIII). When both artery and contiguous vein are injured, a so-called arterio-venous aneurysm may develop.

Results of Recent Injury.—Partial injury of the vessel wall with laceration of the inner layers, although unattended with hemorrhage, may lead to gangrene of the peripheral parts as a result of thrombosis and embolism. Usually, however, hemorrhage is the first sign of vessel injury.

We may distinguish between internal and external hemorrhage depending upon whether the blood appears outside of the body, or not. The blood can be extravasated into the tissues which it may destroy by compressive and extensive forces, and form a spurious aneurysm.

The degree of hemorrhage depends upon the size of the vessel, and that of the wound. If the blood does not find an exit externally, cessation of hemorrhage usually follows by reason of the pressure of the accumulating extravasation; this may occur even without thrombosis. On the other hand, the infiltration with blood may continue into the muscles of the thigh and gluteal group until exitus occurs.

Bleeding from the veins is not as dangerous as the arterial, and more easily arrested through compression bandages.

Another immediate sequence of injury to the veins is *air embolus*. This may occur at operation, or especially as the result of bullet or war wounds. Where the diagnosis can be made, the symptoms preceding death are pallor, slight cyanosis, spasms of the facial muscles, sometimes opisthotonos and cessation of respiration. A peculiar murmur through the vein wall is a significant sign of the entry of air.

Thrombus formation in the vessels implicated in war wounds is not as common as is supposed, at least as far as larger vessels are concerned. Borst² believes that even larger tears and perforations may occur in vessels without thrombus formation. Late thrombosis may occur in parietal or obturating fashion, and then is said to bear some relation to secondary infection. As pointed out in the Chapter on Thrombosis there is still much discussion as to the rôle of infection in the production of thrombosis. Stich reports extensive thrombosis in larger arteries that he exposed because of the fear of secondary hemorrhage in cases of bullet wound injuries.

¹ Salzer, Wien. med. Wchnschr., 1884, No. 89.

² Borst, in Borchard-Schmieden, Lehrbuch d. Kriegs chirurgie, Barth. Leipzig, 1917.

Where infection is associated with thrombosis as the result of blood vessel injury, rapid extension of the thrombotic process not only in the arteries, but in the veins may continue without interruption even into the common iliac or inferior vena cava.¹ Where the thrombotic process is not sufficiently extensive to cause gangrene, other grave sequelae may occur, amongst which may be numerated the following: Recalcitrant edemas, severe paresthesiæ, and marked functional impairment of the limbs.

When the circulatory symptoms are of milder degree, the patients complain of a feeling of coldness, formication, and numbness. Compression through extravasation of blood may cause symptoms without implication of the larger arteries themselves, the hemorrhage occurring from smaller vessels.

Spasm of the vasoconstrictors (Chap. XCIII) has also been observed following bullet wounds in the neighborhood of large vessels. As an example may be cited a case of Kroh.²

After an infantry wound of the inguinal region, a soldier complained of numbness and formication in the foot. The femoral pulse above the bullet wound was barely perceptible. The skin below the knee, inclusive of the toes, was yellowish white, cold, anemic, insensitive to touch and to needle pricks up to the region of the upper calf. The pulse on the healthy side was strong and full. A diagnosis of vasomotor spasm was made, and massage and elevation were ordered. Nine hours later sensibility and pulses had returned to the normal.

In another case the same author demonstrated at operation that the vascular sheath was infiltrated with blood, but not opened. When the femoral artery was exposed, its caliber was about that of a knitting needle, but under the observation of the operator it gradually returned to normal.

Complications.—The most frequent complications are nerve injury or neuritis, pressure effects upon neighboring nerves or irritative phenomena. In view of the proximity of nerves and larger arteries, it is comprehensible that sensory disturbances are frequently associated with vessel injuries. The proximity of the ulnar and median nerves to the brachial artery accounts for the well known combination of vascular and nerve symptomatology. In bullet wounds in this region, the following symptom-complex is not uncommon: the extremity becomes cold and cyanotic, hyperhidrosis develops, and later muscle atrophies and contractures, giving a picture not unlike that of ischemic contracture.³

Some authors emphasize that actual organic implication of nerves is altogether responsible for the vasomotor and contracture symptoms. On the other hand, there are data available which suggest that the arterial lesions and involvement of the periarterial sympathetic plexuses or nerves may give similar clinical pictures (Chap. XCII).

Severe *circulatory disturbances*, usually of the upper extremities may attend bullet wounds of large arteries and lead to *ischemic contracture* of the muscles, without gangrene. Bier reports a number of cases in the upper extremity, usually after injury to the brachial artery. The following example may be quoted.

Bullet wound of the brachial artery of the right arm in a young lieutenant was followed by severe contracture of the muscles of the forearm. About 6 years later the following was the status: The musculature of the forearm was "stony" hard, and only slight motion was possible in the stiff fingers, the wrist joint being ankylosed. The hand was cold, the sensation undisturbed, except in the ulnar territory, and the elbow joint mobile. The fingers were in a position of marked flexion, and discolored bluish red; the peripheral pulses were imperceptible.

¹ See discussion of the stagnation thrombi associated with embolism when infection is present, Chap. LXXXV.

² Kroh, Bruns. Beitr. z. klin. Chir., 1917, 108, 61.

³ See case of embolism of the brachial artery operated upon by the author, in which such symptoms developed, pp. 495, 496.

The *lesions of ischemic degeneration* following ligation of large or main arteries of a member have been described (Leriche and Policard¹) as including the following: In the marginal zones between regions poorly and adequately supplied with blood (1) an absence of all inflammatory phenomena; (2) characteristic changes in the small arteries and arterioles, namely, degeneration of the muscular elements of the media with conservation of the connective tissue.

In the ischemic territories the following muscle alterations are worthy of emphasis: (1) a rapid degeneration of the muscle fibers that attains a certain degree at which the process is held in *statu quo* over a long period of time; (2) segmentation of muscle fibers in discs and the disappearance of nuclei; (3) augmentation of the amount of fibrous connective interfibrillar and interfascicular tissue, the nuclei here also being lost.

Injury of a Main Artery or Vein.—Wounds of large arteries give rise to symptoms that vary according to whether there is a sufficiently large wound to permit of the escape of the blood, or whether infiltration of the deeper tissues with the escaping blood takes place, with the formation of a hematoma. When one of the chief vessels of an extremity is torn, the peripheral portions of the limb, become pale, cold, somewhat insensitive to pain or anesthetic. These manifestations may persist, or be evanescent. As a rule, the collateral circulation becomes rapidly established, and it is only in rare cases that gangrene follows an arterial injury, or wound, when the blood can escape externally. However, when the tissues are infiltrated, and a large hemorrhagic exudate is formed, gangrene is more frequently the issue.

Interesting and instructive observations could be made on the results of injury of the femoral artery during the Great War. Only in some cases did gangrene develop.

When there is an open wound of the thigh involving the *femoral artery or vein*, lethal bleeding takes place so rapidly that surgical aid rarely, if ever, comes into play. Where the entering body is small and takes an oblique course, closure of the external wound may take place, and by virtue of deep hemorrhage the collected masses of blood may by great pressure, bring about a cessation of the hemorrhage. Small holes in the femoral arteries may heal spontaneously or lead to the development of traumatic aneurysm.

Late or secondary hemorrhages and secondary erosion of the vessel wall may lead to grave consequences.

Symptoms.—The thigh is enormously swollen and tense. Large hematoma can spread in the direction of the scrotum and perineum. Characteristic is the pulsation which when it can be elicited over the hematoma, gives the picture of a pulsating hematoma. With this there may be absence of the pulse in the dorsalis pedis and posterior tibial, circumstances that make a diagnosis of injury of the femoral artery certain. However, the presence of pulsation in the vessel does not necessarily indicate an intact femoral artery. Within a few days a typical *bruit* can develop and this may be either systolic or systolic-diastolic, when an arteriovenous aneurysm is present.

Associated with the swelling are severe pain and paresthesiæ, due either to injury to the nerves themselves or to their implication in the bloody exudate.

Secondary hemorrhages may take place through the bullet tract, and these are of grave import.

Secondary infection also may give concern, and may occur early within a few days or late, even after a week.

¹Leriche and Policard, Compt. rend. Hebd. de la Soc. de Biol., 1920, p. 415.

CHAPTER XXXVII

ANEURYSMS

Pseudo-aneurysms.—A false aneurysm or pulsating hematoma may result from a condition in which an extravasation of blood remains in communication with an injured artery. Other appellations recently given to this condition are *communicating* or *pulsating hematoma*. By some authors this is described as a transitional stage in the development of a traumatic aneurysm, for in a few weeks the hematoma may become distinctly demarcated and circumscribed against the surrounding healthy tissues, and become converted into an aneurysm.

These pseudo-aneurysms or pulsating hematomata vary in size, depending upon the caliber and situation of the injured vessel; also upon the size and the form of the vascular wound, the initial treatment given, and the circumstances attending the transportation of the patient. Thus, it has been observed that relatively small vessels such as the radial artery give rise to hematomata that are as large as those of subclavian origin. Pulsating hematomata are usually larger in the case of arteries, than when a simultaneous injury of artery and vein occurs.

Nor is there a constancy in the size of the hematoma. After cessation of hemorrhage a shrinkage of the mass is observable due to resorption of blood; or, by reason of increased pressure after exertion, constipation, or other mechanical influences (sneezing, defecation) late hemorrhage into the sac may occur with enlargement of the mass. Or, infection of the sac may bring about similar changes in volume.

With the coagulation of the blood a stratified or onion-like deposition of coagula takes place in the hematoma with white, red, and mixed thrombi. Those masses that are in immediate apposition with the tissues become organized first, and constitute the sac of the aneurysm, whereas the more centrally situated contents are masses of cruor, blackish, reddish blood of varying consistency. It is remarkable that the circulation may continue in spite of the communicating thrombotic and cruor masses. Indeed, even the peripheral pulses may be conserved.

Anatomically the pseudo-sac is made up of a thin fibrinous membrane, composed of homogeneous fibrin enclosing leukocytes and red blood corpuscles. There is no endothelial lining in all of the recent cases.

Traumatic Aneurysms.—For a comprehension of the circulatory disturbances of the extremities only the salient features of these types of aneurysms and their rôle in the production of vascular disturbances require mention here. Further data with surgical bearing must be sought in the surgical literature.

A traumatic aneurysm is produced by virtue of encapsulation of a pulsating hematoma. A distinction has been made between *false* and *true* aneurysms. The former designation has been applied to aneurysms arising in consequence of injuries to a normal vessel wall through dull or sharp force; the latter has been referred to circumscribed or circumferential dilatation of the vessel. A distinction has been made between two varieties; *false* aneurysms in which there precedes a defect in the wall of the vessel, and *true* aneurysms that are still lined with an attenuated and dilated wall. Some authors would extend the term, aneurysm, so as to include all dilatations

irrespective of whether they develop spontaneously or after traumatic lacerations.

The terms diffuse false aneurysm and circumscribed false aneurysm are found in the literature descriptive of recent arterial injuries on the one hand, and older encapsulated products on the other hand. Another appellative, encapsulated hematoma, either pulsating or non-pulsating has been suggested (Schum).

Symptoms.—Only those features concern us here that relate to the circulatory disturbances occasioned in the affected extremity. Referring briefly to the general symptomatology, this may be summarized as follows: first, tumor formation brought about by the presence of one or more partly or completely organized blood sacs arising from the vessel; second, a pulsation of this sac synchronous with the arterial pulse; third, a murmur synchronous with the cardiac systole; fourth, circulatory disturbances in the peripheral course of the artery and its branches with changes in the peripheral pulses; fifth, manifestations due to implications of accompanying nerves (irritative phenomena of the sensory fibers, paraesthesia pain, paralytic symptoms) with involvement of either motor or sensory fibers; and sixth, contractures implicating neighboring joints.

We shall dwell only upon those circulatory and neurogenic disturbances that are germane to the subject matter in hand here.

Circulatory Symptoms.—The peripheral pulse may be felt beyond the site of the aneurysm, or may be absent due to complete occlusion of the artery, because of compression of the artery by a sac against non-yielding supports, such as bone; or due to kinking of the arterial channel from overdistension of the sac and the direction of its growth. When a pulse is present, it may be diminished as compared with the healthy side.

Complications and Gangrene.—The most important of these is hemorrhage which can occur externally or into the tissues, particularly in traumatic aneurysms. Late secondary hemorrhage is not uncommon and a not infrequent cause of a lethal outcome. Indeed, it may occur from the first to the fifth week, or after 2 months.

The symptoms of internal bleeding are the following: increasing pain in the extremity, paraesthesia, swelling edema. As the result of the compressing action of the hematoma, ischemic contractures, disturbances in the nutrition of the whole extremity, and even *gangrene* may occur.

CHAPTER XXXVIII

TREATMENT OF INJURIES TO THE BLOOD VESSELS

In recent injuries of the blood vessels, our aim should be a two-fold one; firstly, the prevention of the immediate danger of the loss of blood; and secondly, the restoration of the circulation of the part.

The Control of Hemorrhage.—Little emphasis need be laid upon the value of the Esmarch rubber tourniquet, for the prevention of hemorrhage from an extremity. Occasionally, it is well to sew up a wound tightly when bleeding occurs from regions inaccessible to an Esmarch or Martin bandage, particularly on the battle field, when complete surgical equipment may not be at hand. If the wound be too large, it may be tamponed very tightly and the skin sutured over it, a pressure bandage being placed over the whole.

These are but temporary measures, and must give way to the permanent or final control of the bleeding through other means.

Another method often suggested is the application of sterile gauze over which compression is exerted through a solid unopened well rolled muslin bandage. This is made to obliterate the arterial lumen through a compressing force brought into play by a firmly applied superimposed rubber bandage. Or, we may be constrained to leave artery forceps in the wound, under certain circumstances on the battle field.

The Permanent Control of Hemorrhage.—The question whether a ligature or suture of the vessel is indicated depends upon the size of the vessel, the condition of the wound, the circumstances under which hemorrhage must be controlled and the presence or absence of adequate surgical material and equipment. During the Great War even some of the smaller arteries were successfully sutured, when a lateral opening was present (radial artery, Stich). Whenever we believe that the ligation of a vessel of moderate size will not compromise the integrity of the peripheral parts, ligation may be carried out.

Given the proper circumstances, an absence of general or local infection, and a patient who is in a condition for suture operation, the question of adequacy of collateral circulation is an important one in determining whether suture or ligature operation should be attempted.

For the investigation of the adequacy of collateral circulation a number of tests have been employed, particularly the Mosckowicz test (Chap. XXIX). This test may be carried out in the following modified manner.

Taking an injury of the femoral artery as an example, the limb is made ischemic either through elevation, or better still, through the application of a rubber bandage, below the point of injury. Thereupon the femoral artery is compressed against the pubic bone until all pulsation below disappears. The rubber bandage is taken off after about 2 minutes, and the limb either kept at the horizontal or preferably depressed. If the collaterals are adequate, a hyperemic reaction takes place up to the tips of the toes in spite of the continued compression of the femoral artery. It must be remembered that it is good to control this test by a similar one on the healthy extremity, and that the findings are only reliable if we are certain that the artery is being properly obliterated by pressure above. The Lexer-Coenen test (Chap. XXIX) also described by Henle and others may give valuable information if it is positive, and the rapid almost pulsating arterial flow from the arterial stump gives evidence of sufficient collateral circulation.

The Relation of Larger Arteries to Nutrition of the Part.—The effects of ligation of the femoral artery have been variously estimated. According to Wolff (1908) the following percentages were given for various larger arteries, as to the incidence of gangrene of the lower extremity after ligation of various large arteries. After ligation of the external iliac 50 per cent gangrene; common femoral both above the profunda 25 per cent; popliteal 40.9 per cent; femoral below the profunda 12.7 per cent. As for the upper extremities, gangrene was noticed after ligation of the axillary artery in 15 per cent; subclavian and brachial about 4.8 per cent.

Treves had already pointed out, years ago, the great risk attending ligation of the common femoral artery. Observations during the late war, however (Sencert) seem to indicate that ligation of the femoral artery is not as dangerous to the vitality of the limb as is commonly believed. This author ligated the femoral 11 times (in 3 the common femoral) with no case of gangrene. Only where there was a large hematoma did gangrene occur (9 examples of the latter).

Heidrick reports that gangrene follows ligation of the femoral in 20.7 per cent of the cases. This author is in accord with the view already expressed

that gangrene is more frequent following ligation below the origin of the profunda than above.

It is important to take into consideration in any interpretation of the consequences of ligation and injury as to the presence or absence of previous arterial disease. Infection, trauma, secondary thrombosis all play a rôle in determining whether gangrene will take place or not.

It must be further remembered that while the skin may be adequately nourished after ligation of a large vessel, this does not necessarily pertain to the subsequent condition of the deeper tissues. It is well known that the musculature is much more susceptible to diminished blood supply than the skin. Therefore, necrosis may take place after ligation, but leave the integument intact. In this way can be explained the sequelae after ligation, and complications that may occur weeks after the operation. Even ischemic contractures have been reported.

Principles Underlying Surgical Treatment.—For details reference must be made to surgical treatises and to the literature in this domain. Certain basic facts and observations, however, that are relevant for an understanding of the circulatory phenomena and conditions in the extremities merely need be dwelt upon here.

It is now believed that ligation should be made at the point of injury, and that both vessel stumps should be cared for. The older admonition to treat and ligate the vessel at the site of predilection is fallacious advice, since it can neither assure one against secondary hemorrhage, nor is it free from the danger of gangrene. Only when the bleeding vessels cannot be found nor sought for in view of the local condition of the wound, is the more remote or indirect ligation permissible.

Ligation is only reliable in healthy tissue, so that it may be necessary to dissect the artery for some distance, isolate it and tie in more healthy territory.

Ligation and Treatment of Aneurysms.—If a pulse beyond the aneurysm is present, one can defer operation, while if the pulse is absent, extirpation can be carried out without any fear of gangrene.

Experience in the late war has taught us considerable regarding the time necessary for the development of collateral circulation. Some authors suggest waiting for several months, while others believe that in a period from 3 to 6 weeks adequate collateral circulation will have become established, so that ligation of the artery can be done without danger. Early operation after rupture of a blood vessel or formation of a traumatic aneurysm may be dangerous, not only because of the absence of collateral supply, but also because of the compressing effects of the hematoma, which may be expected to become absorbed after sufficient delay. The danger to collaterals is thus automatically and gradually removed.

Whenever ligation of an artery or extirpation of an aneurysm is done, it is important to inspect the more peripheral parts of the extremity, as regards the circulation, and to obtain a knowledge regarding the condition of the collaterals. If the extremity is of good color after temporary compression of the afferent artery (leading into an aneurysm) ligation can be carried out without fear. If there is doubt, some authors advise small incision into the periphery of the extremity, so as to determine whether bright blood, dark blood or none is evacuated. If after from 10 to 15 minutes of observation, the extremity is still pale, or has a marmorated appearance, then we can conclude that the collateral circulation is inadequate.

Furthermore, the data furnished by the Henle-Coenen collateral sign (Chap. XXIX) are of importance. Considerable discussion has arisen as

to the advisability of simultaneous ligation of the accompanying large vein, when a large artery is ligated. In the case of arteriovenous aneurysms, this matter requires no special decision. When suture is possible, both may be conserved; if not, and extirpation has to be done, both have to be ligated. When the vein, however, is intact, certain data on observations during the Great War would point to the advisability of ligating the vein.

Thus Wolff¹ reports that after ligation of the femoral artery alone, there were 20.7 per cent cases of gangrene, while if the vein also were ligated, only 8 per cent. In the case of the upper extremities, ligation of the arteries 7.8 per cent, ligation of both artery and vein—no cases of gangrene. Many theories have been propounded regarding the explanation for this phenomenon. According to some, a disproportion between collateral afferent supply and venous outflow is avoided by ligation of the vein. Johannessen² published a case in which the lower extremities evidenced very poor circulation after ligation of the femoral, edema and pain. After the vein was ligated, 8 days subsequently, a continued improvement in circulation occurred.

On the other hand, deleterious consequences have followed ligation of the femoral vein. According to the statistics of Braun,³ the ligation of the femoral vein alone, above the profunda produced gangrene in 2.8 per cent of the cases.

Indeed, some authors advise against ligation of the femoral vein, because of the likelihood of stasis. On the whole, although there are dissenting voices, the majority of surgeons rather favor the simultaneous ligation of the artery and the vein, with certain exceptions in the case of the lower extremities. It is well in each and every case to decide this at the time of operation, when by temporary arrest of the circulation of the vein, observations can be easily made as to whether the circulation is objectively improved thereby.

Neurovascular Syndromes after Ligation of Large Arteries.—There is a clinical complex that either temporarily or permanently restricts the muscular activities, when impairment of the circulation of a limb follows ligation of one of the larger arteries. It is not surprising that a diagnosis of malingering is often made, for, while under the observation of the physician, little is objectively in evidence. However, upon increased activity and work, especially if the latter is excessive, and also under exposure to cold and moisture, circulatory disturbances appear. These are coldness and blueness of the hands and feet, reduction in the size of the pulses, rapidly developing edema, a sensation of numbness in the extremities, and occasionally dull pain. When the limb is put at rest, both objective and subjective manifestations appear.

It would seem, in light of experiences during the Great War, that reestablishment of the circulation through suture of the artery involved would prevent the development of these clinical syndromes. The favorable results obtained by von Haberer with arteriorrhaphy, as compared with ligation, definitely demonstrated the advantages of the suture method.

Arteriorrhaphy.—Opinions are not in accord as to the value of vessel suture after injury, some tending to the extreme that the method has little or no useful sphere of application, while the other schools employ it *even in the presence of infection*. It appears to the author that arteriorrhaphy, when carried out by those sufficiently skilled and with careful technic, is an exceedingly useful procedure that will receive more and more recognition, as the experience of the surgeons in this work increases.

¹ Wolff, Brun's Beitr. z. klin. Chir., 58, 762.

² Johannessen, Zentralbl. f. Chir., 45, 516.

³ Braun, Arch. f. klin. Chir., 28.

The procedure is to be entertained in view of the following dangers of ligation; firstly, the vascular and neurovascular remote consequences; and secondly, the dangers of gangrene.

Certain authors report successes even in infected tissues, so that the view oft accepted that scrupulously clean fields are essential, may have to be rejected.

Among such instances may be mentioned the case of Danielsen¹ of suture of the axillary artery in infected tissues. V. Haberer² described 7 cases of arterial suture with healing in the presence of severe local infection; and Schoene³ closed a longitudinal slit in the popliteal artery in the presence of a gas phlegmon, with a pulsating posterior tibial artery (!) as a result.

The danger of gangrene consequent upon suture is less than that following ligation. The immediate reestablishment of circulation, however, after suture does not preclude the possibility of late gangrene. Such has been reported as taking place 2, 3 or 6 weeks after the operation, usually gradually but in some instances suddenly. In such cases the outcome is due to secondary thrombosis.

The mild circulatory disturbances that are most apt to occur after impaired circulation due to arterial injury and ligation are less frequently observed after suture, or in much milder form. These disturbances are the following: a feeling of coldness, sometimes paresthesiæ, sensations of heaviness, numbness and formication. In some patients pain occurs after bodily exertion, or a hard edema of the affected limb may ensue. It is the opinion of v. Haberer and Stich that objective and subjective disturbances are usually absent in those cases of arteriorrhaphy where the peripheral pulses were reestablished after the operation. It has already been pointed out that peripheral pulses may return weeks after arteriorrhaphy, due to the intervention of collaterals, so that only the immediate restoration of the pulses can be regarded as an evidence of a successful reestablishment of the arterial paths.

CHAPTER XXXIX

THROMBO-ANGIITIS OBLITERANS—INTRODUCTION

It seems strange that a primarily scientific study of the lesions of thrombo-angiitis obliterans—later supplemented by clinical observations—should have laid the foundation for a correct appreciation and classification of a large number of affections involving the circulation of the extremities. Indeed a careful consideration and investigation of all the basic anatomical changes as well as the many clinical phenomena characteristic of thrombo-angiitis obliterans, will do more in a practical way to fashion and shape our concepts of the vasomotor and trophic neuroses and all allied organic affections of the vessels of the limbs, than the study of any other single or group of such diseases. And this is true because manifestations of almost all of the morbid conditions in question are represented in this one interesting malady.

The medical student as well as the practitioner whose diagnostic appreciation of Raynaud's disease, erythromelalgia, chronic acrocyanosis, athero-

¹ Danielsen, Deutsch. Ztschr. f. Chir., No. 11, 40, 381.

² v. Haberer, Arch. f. klin. Chir., 108, H 4.

³ Schoene, Deutsch. Ztschr. f. Chir., 1918, 143, 84.

sclerotic vascular lesions, and thrombo-angiitis may still be obscure in spite of reading of text books or of clinical experience, will find his doubts and clinical obscurities remarkably clarified by an intensive study of the varied manifestations and lesions of thrombo-angiitis obliterans. It is for this reason, that the author has deemed it wise to indulge in a comprehensive discussion of its pathology, its latent and active symptoms.

CHAPTER XL

THROMBO-ANGIITIS OBLITERANS—GENERAL CLINICAL CONCEPT

Thrombo-angiitis obliterans¹ is a clinical and pathological entity which has been, and is still, incorrectly called "endarteritis obliterans" by many authors. The names, presenile, and juvenile gangrene have also been applied to it.

At the onset, thrombo-angiitis obliterans is essentially an inflammatory process, involving particularly the deeply situated and larger arteries and veins of the lower and upper extremities. Almost immediately after the inception of the lesion, there follows extensive occlusive thrombosis, that subsequently gives way to a stage of healing or organization, the final result being the complete closure of arteries and veins over a large extent of their course by vascularized and canalized connective tissue. Although no extensive study has been made of thrombo-angiitis in the vascular domain outside of the extremities, the typical lesions have been observed by the author: in the spermatic vessels, and according to Murphy, are said to occur in the renal vessels.

Characteristic is the involvement of the superficial veins, of the lower and upper extremities in the form of a *migrating* or *thrombo-phlebitis* in about 20 to 25 per cent of the cases. It is in this territory that the most thorough and reliable investigations on pathology can be made, as the lesions in the vessels then become accessible at the very onset of the malady before the effects of organization and healing have confused the histological picture.

Clinical and Pathological Concept of Thrombo-angiitis.—The disease manifests itself in most instances with indefinite pains in the sole of one foot (usually the left) in the ankle, or in the toes, the patients being soon disturbed in their walk by these symptoms, or by the sudden onset of cramp-like sensations in the calf or elsewhere in the leg (intermittent claudication). These feelings make the patients take frequent rests, often inducing them to investigate the condition of their limbs. Some take off their shoes and rub the part in the hope of dispelling the pains or banishing the uncomfortable numbness of the toes and feet; others say that the feet become cold and numb when the temperature is low and the weather is inclement. After the lapse of weeks, months or even years, evidences of *trophic disturbances* make their appearance. Following the cutting of a nail, or without apparent cause, an abraded spot or hemorrhagic bleb, a pustule, or a dry, dead patch of skin develops near the

¹ This name was suggested in 1908 by the author for this interesting and remarkable disease and has been almost universally accepted in the United States.

tip of one of the toes or under a nail. Now the local pain becomes excruciating during the night as well as day, so that some of the sufferers beg for amputation of the affected part.

It is usually during the first attack of trophic disorder, but sometimes when only intermittent claudication is present, that the physician or patient notices another characteristic symptom, namely, a peculiar blush of the toes and forepart of the foot, sometimes extending to the ankle or slightly above, when the limb is in a pendent position (Plate IV). Upon allowing the limb to hang down, the affected toe soon turns color. It assumes a bright red hue which is seen to pass to the other toes and then up the back of the foot



FIG. 46.—Trophic lesions in thrombo-angiitis obliterans.

for a variable distance. This reddening is often termed *rubor*, or may be called *erythromelia*. The elevated extremity on the contrary, rapidly becomes blanched (ischemia). Sometimes the superficial ulcer will heal under conservative treatment and the patient will either recover perfectly or his symptoms will become chronic. At this period his limb may show the trophic lesions and scars left by previous ulcers (Fig. 46). The dorsalis pedis and the posterior tibial arteries usually fail to pulsate, and ischemia in the elevated position and redness of “erythromelia” in the pendent position are regularly

elicited. Sooner or later, however, a patch of gangrene develops, the local pain becomes intense, and amputation will be the issue.

Because of the striking condition of redness in the dependent position, and because of the increase of local pain when the limb is hanging down, a number of clinicians have been accustomed to diagnosticate "erythromelalgia" in these patients. Some cases have been regarded as examples of Raynaud's disease, because in them the symptoms of blanching and cyanosis of the parts were prominent features. Although resembling erythromelalgia and Raynaud's disease in a number of symptoms, the clinical picture of thrombo-angiitis obliterans is so characteristic and definite, and the pathological lesions so typical in this disease, that it constitutes a distinct clinical entity.

A general concept of the disease could be briefly formulated in the following terms. Imagine a patient seeking relief for acutely swollen superficial veins of the lower or upper extremities, of sudden advent, and with all the manifestations of an acute thrombo-phlebitis. Imagine this process involving a considerable portion of the distal territory of the internal saphenous vein, followed by abatement of symptoms, and consequent resolution or healing. You will be in no doubt as to the general pathology nor as to the clinical course of the condition, though your estimation of the etiology will in most instances, at least be obscure.

Transfer this picture to the deeper vascular system, over the distribution of the external and internal plantar arteries and veins, the dorsalis pedis, anterior tibial, posterior tibial and the perineal arteries and veins, that is, with lesions in territories where objective manifestations are absent—and you will be depicting to yourself, what corresponds to our own conception of the pathological process in the disease, thrombo-angiitis obliterans. So here, too, we postulate, an acute inflammatory and thrombotic lesion, but one involving deep arteries or veins, or both, as the initial stage of the pathological anatomy.

Whereas, the patient afflicted with an inflammatory and thrombotic lesion of the superficial veins presents objective signs easy of recognition, the patient suffering from thrombo-angiitis obliterans in its earlier stages may offer no objective evidences suggestive of the true nature, or of the site of the lesion. It is but in a very few cases that one is justified in ascribing certain symptoms to the incipient stage of the disease. Severe, non-localizable shooting pains in the calf or foot, attended with difficulty in walking, or, possibly with tender calf muscles, with or without vasomotor symptoms and coldness in the foot, with or without obliteration of the dorsalis pedis and posterior tibial pulses, may be the only symptoms. It is only when we compare the history with the future clinical course and pathology that we can relegate such indefinite signs to the onset of the affection. In most instances, however, the patient will not seek advice for such initial symptoms, either because they are not sufficiently severe to require the attention of a physician, or because they are incorrectly regarded as rheumatic in origin, possibly due to trauma, cold, the presence of flat or weak foot, or because they are explained on the basis of some other minor ailment.

Strange to say, patients afflicted with thrombo-angiitis obliterans may present symptoms which differ in no way from those attending the thrombo-phlebitis of the superficial veins, or so-called migrating phlebitis. These are the cases of thrombo-angiitis obliterans in which an acute inflammatory thrombosis involves smaller or larger portions of the external or internal saphenous vein, radial, ulnar, median cephalic or median basilic vein. Such

over to 218

PLATE IV



Erythromelia or Rubor in Thrombo angiitis Obliterans. (Buerger in Ochsner's
"Surgery," Vol. IV.)

cases are the most instructive of all, for they are the ones which afford us material for pathological study. Here the veins are accessible; portions can be surgically removed when the lesions are in the acute inflammatory stage and submitted to histological examination.

While the former type of cases is difficult to diagnose, the variety with concomitant migrating phlebitis can be recognized by a study of the vein lesions under the microscope. If the tissue be examined when the lesions are still in the early inflammatory stage, before organization or healing has taken place, certain characteristic and specific lesions can be identified, changes which shall elsewhere be described as pathognomonic for thrombo-angiitis obliterans.

Having learned that the incipient lesion of thrombo-angiitis obliterans is an acute inflammatory one, involving the arterial and venous walls, we will expect an occlusive thrombosis as the immediate sequence, and will not be surprised to find that this stage gradually gives way to one of organization and canalization, resulting in a healed product in which the vessel becomes converted into a cord, more or less adherent to its surroundings, and in which even the neighboring nerves may become agglutinated and enveloped in a fibrotic vascular cord.

It is the interference with the circulatory conditions of the limbs brought about by the extensive occlusive process that is responsible for most of the clinical manifestations of thrombo-angiitis obliterans. *So that it may be correctly said that patients afflicted with thromb-angiitis obliterans do not usually suffer directly from the disease itself but from the disastrous occlusive thrombosis which signalizes Nature's method of healing a vascular lesion that has long since disappeared.*

From a study of the pathological material, and from a comparison of the lesion with the clinical history, we must conclude that insidious or clinically unrecognizable exacerbations of the lesion may occur from time to time, so that the involvement of the vascular territory with the obliterative lesion is a progressive one until the summit of the organized clot reaches the popliteal, in rare cases the femoral or even the iliac arteries. It will not occasion astonishment, therefore, that clinical manifestations, too, become more and more serious as time goes on.

Nor must we be surprised if thrombo-angiitis obliterans simulates clinical complexes brought about by arterial occlusion from other causes. Differentiation from arteriosclerosis, endarteritic occlusion, and other thrombotic conditions may at times be difficult. It is the fact that thrombo-angiitis obliterans occur in *very young individuals* in whom both the vis-a-tergo and the cardiac power are adequate for compensation, and in whom the vascular adaptability is elastic in its scope—it is this fact that accounts for the seemingly almost inexplicable circumstance that gangrene occurs *so late*, or may be absent, in spite of vast and extensive obliteration of arteries and veins. It is to the development of the collateral circulation, therefore, that we owe, in part at least, the production of a very peculiar, striking, and characteristic clinical picture, recognizable even though manifestations of the acute stage of the disease, or manifestations, such as migrating phlebitis are absent.

CHAPTER XLI

THROMBO-ANGIITIS OBLITERANS—ACUTE STAGE

More interesting than the study of the usual manifestations, due to impaired circulation, is the investigation of those phenomena that are clinically referable to the "acute stage," that correspond to the acute inflammatory invasion of the deep arteries and veins. As elsewhere pointed out, when the patient seeks advice, he no longer suffers from the affection thrombo-angiitis *per se*, but from the "healed stage" (in the pathological anatomical sense) where the vessels have discarded their inflammatory products, have become converted into hard fibrous cords, and are only in so far responsible for the clinical picture, in that their function as conductors or vascular channels is completely in abeyance, the symptoms being altogether due to a "lack of circulation" or a mechanical interference with the delivery of blood. A diligent search for manifestations attributable to the attacks of deep thrombo-angiitis or thrombo-phlebitis may find its reward in the discovery of treatment or prophylaxis, available and applicable *before extensive closure of vascular channels has taken place. Such is the importance, then, of the recognition of signs that may be interpreted as coincidental with the onset of acute lesions.*

The Acute Symptoms.—These, as far as the author has been able to detect, are *lancinating pains* in the legs, especially in the calf and foot, *cramp-like pains* in the leg first interfering with walking, later requiring complete rest, *tenderness* in the calf and along the anterior tibial region, simultaneously with, preceded by or unassociated with attacks of migrating phlebitis. These manifestations may last for a variable time, are unattended with trophic disorders, but accompanied by development of ischemia on elevation *without* or with evidences of disappearing pulses. When the closure of the vessels is confined to the peroneal, and distal vessels such as the plantar and peripheral distribution of the anterior tibial artery, and even when a portion of the anterior tibial high up is involved, the posterior tibial in its usual situation behind the malleolus and the dorsalis pedis may be found pulsating.

The suddenness of the onset of pain in both legs with the absence of true intermittent claudication at the incipency of the trouble, with the slow appearance of the usual signs, justifies the assumption that a period due to "acute involvement of the deep vessels" was here exemplified in the clinical examples at hand. Observed carefully from the stage where *none* of the objective signs of thrombo-angiitis obliterans were associated with attacks of pain in the calf and leg, up to the time when distinct manifestations could be recognized, the following case permitted of the clinical separation into first a stage of acute thrombo-angiitis obliterans, with symptoms referable to the disease *per se*, and a second stage that of symptoms due to arterial obturation, *a period usually regarded as representative of the disease itself.* (Cicatrical stage; stage of *mechanical hydrostatic and then trophic disorders.*)

N. S., male, Russian Hebrew, age 26, August 28, 1916, began eighteen weeks ago with *sudden severe cramp-like pain* in the calf of the left leg radiating upward into the thigh. This was treated as sciatica in one of the hospitals without improvement. Soon thereafter a similar attack occurred in the right leg which made walking difficult. There were no external noticeable changes to account for the trouble. Physical examination revealed *no* ischemia, no rubor, none of the signs of thrombo-angiitis obliterans, other than doubtful pulsation in the dorsalis pedis arteries.

December 11, 1916 (about three months of continued difficulty in walking) in the region of the left calf, along the course of the peroneal and posterior tibial arteries, there was *marked tenderness*; no change in the pulsations but *ischemia now marked*; so also *reactionary rubor* with rather distinct cyanosis in the pendent position.

January 2, 1917. Now there is no doubt as to the absence of the dorsalis pedis in the left leg. In short, first a stage of pain without further symptoms; second the development of tenderness in the calf corresponding to the course of the vessels with some cyanosis in the pendent position, and third, the development of *ischemia*, *reactionary* erythromelia and pulseless dorsalis pedis artery.

Although in the main, it is a difficult matter to recognize the symptoms that are referable to the acute process in the deep vessels, certain symptoms have been noted in a number of cases, that were sufficiently suggestive to warrant being interpreted as due to the deep thrombosis and inflammation.

M. P. gave a previous history of migrating phlebitis for which he was admitted to the Mt. Sinai Hospital. On May 24, 1908, a physical examination was made by the author. He had been in the hospital once before, on August 15, 1907, for phlebitis migrans. He was again suffering from an attack of phlebitis now involving the saphenous vein and its tributaries to the middle of the left leg, and also the ulnar vein near the left wrist. *Now for four days he had had paroxysmal attacks of deep pain in the right leg* especially in the region of the calf, not attributable to the superficial parts. Neither the dorsalis pedis nor the posterior tibial artery could be felt pulsating. These attacks were carefully observed. There was no apparent cause for them; and it is more than likely that they were due to inflammatory thromboses of the deep vessels, similar to those involving the superficial veins. The gradual development of erythromelia and moderate ischemia in the elevated position, were corroborative signs. Although the pain had disappeared after four days, the rubor persisted.

The future course confirmed the suspicion of involvement of the deep vessels, since in 1909 trophic disturbances of both feet developed, and amputation of the right leg became necessary; in 1911 the left leg was also lost through amputation.

CHAPTER XLII

THROMBO-ANGIITIS OBLITERANS—CHRONIC STAGE

It is only through a knowledge of the vicissitudinous paths followed by the sufferer with this disease in his quest for a cure, and by a study of the diversity of combinations that the usual manifestations may present, that a comprehensive understanding of the mutations in the pathological process and of the prognosis can be obtained. But a relatively few of the manifold types will be mentioned here; the affection as it is associated with migrating phlebitis (Chap. LVIII) and as it involves the upper extremities (Chap. LIX).

1. *Cases without Trophic Lesions or Gangrene.*—By these, we mean that certain patients exhibit merely the usual subjective and objective manifestations of impoverished circulation over years of clinical observations (2–10 yrs. or more), but may at any time thereafter be afflicted with ulcers or a mortifying process. For years, with or without attacks of migrating phlebitis and intermittent claudication, chronic rubor develops, the foot is distinctly blanched on elevation, the dorsalis pedis and posterior tibial pulses are absent (sometimes the popliteal) but trophic disorders do not appear.

2. *Cases of Exquisite Chronic Rubor*, with dystrophic changes, loss of merely one or more phalanges after 16 or more years of suffering (case D. B.),

deceive the prognostications of the clinician. After prodromal phlebitis of either upper or lower extremities recurring for years, coldness, cyanosis and pain with chronic rubor develop, so that a painful limp is established, a phalanx or more may be lost, but the limb, except for slight edema, puffy toes and angry red color, appears intact. This picture is analagous to that of chronic pseudophthisis or chronic (vascular) atrophy with rubor described as characteristic of arteriosclerotic vascular occlusion. In the former, however, the age of the patient, the migrating phlebitis, the puffy toes, the swollen rather than withered foot, are distinctive differential points (case D. B. Chap. LVIII, p. 287).

3. *Trophic Lesions the First Symptom.*—As shall be pointed out elsewhere, the disease may be present in a latent form in either or in both lower extremities, so that it may happen that the patient believes himself well until a blister appears (big toe in case D. K.), the toe and foot become red and painful. Objectively, erythromelia is marked, the usual pulseless vessels are demonstrable, a trophic ulcer has developed, and gangrene is imminent.

4. *Cases of Short Duration (Acute and Subacute).*—Although the usual course of the disease is a chronic progressive one with a long prodromal period, then the gradual development of trophic disorders and finally gangrene, there are cases in which very rapid development of gangrene can take place. It is barely possible that the initial symptoms are not noticed, their development being insidious and too slight to warrant attention. Thus:

M. G., 35 years of age, Russian Jew, apparently well until four months before examination (June 30, 1909), noticed coldness of the left foot and then pain in the toes which rapidly became so severe that it was necessary after some two months to go to bed. Now, four months after the onset of the disease, the big toe of the left foot has become black, and the tips of the fourth and fifth toes are also becoming mortified. At the time of examination there were distinct evidences of gangrene of the fourth and fifth toes, absence of pulsation in the dorsalis pedis and posterior tibial vessels, and the usual signs of thrombo-angiitis obliterans. Within a few days amputation became necessary.

In short, within about four months the disease ran a complete course with the loss of one limb.

5. *Sudden Gangrene Simulating the Embolic Type.*—Although the development of gangrene is usually a slow process passing through the stages of superficial necrosis, ulcer formation and then gangrene of one toe at a time, in rarer instances after a period of the usual preliminary subjective manifestation, upon cutting a nail or apparently without cause, extensive gangrene of several or all the toes including the forepart of the foot may develop *within a very few days*. Such a course would indicate that either a fresh accession of thrombosis took place in many arteries with inadequate opportunities for the establishment of collateral paths, or that an involvement of the popliteal cut off the collaterals upon which the nourishment had previously depended. When seen with gangrene well established, the clinical picture is confusing, simulating mortification of embolic, thrombotic and arteriosclerotic processes.

6. *Cases without Symptoms.*—Very frequently the disease is overlooked by the patient in one limb, whilst it is active in the other, or has existed for years in one leg, remaining *unnoticed until the advent of the more serious and distressing manifestations* calls his attention to the affection *in the other limb*. It is not uncommon to find on examination of a case presenting the typical objective phenomena in one extremity, that the other leg is the seat of the same disease, physical examination revealing signs of extensive arterial obliteration and signs of occlusion of many vessels. Other objective phenomena, too, warrant the assumption of an insidious onset with subsidence of the acute lesions, and the establishment of adequate collaterals. To cite a case:

M. P., the supposedly *healthy leg* evidences marked redness of the big toe and adjoining region with some ischemia on elevation, and with the appearance of cyanotic patches over the tips of the toes. Reactionary erythromelia is pronounced, being a phenomenon never seen in a healthy leg.

The dorsalis pedis, posterior tibial and popliteal arteries are pulseless.

Comparing this type of involvement with that of the other leg in which the objective manifestations were more pronounced, we find the following in the latter. First, marked erythromelia even in the horizontal position varying in intensity, there being a play of colors such as is seen in the vasomotor cases. Alternating rubor with patches of ischemia is seen, the red color predominating. Second, the tumefied condition of the foot with the disappearance of the normal irregularities. Third, the markedly cadaveric appearance on elevation. Fourth, the very slow return of color on depressing the foot after previous elevation. Fifth, the extreme descent below the horizontal necessary before any color returns in the foot (small angle of circulatory sufficiency).

From this we may conclude: First, that both legs may be intensively involved with thrombo-angiitis obliterans, one of them alone giving subjective symptoms; secondly, that extensive obliteration of the vessels as manifested by the absence of pulsations in the dorsalis pedis, posterior tibial and popliteal arteries may occur without symptoms; and thirdly, that certain physical signs, however, can be elicited, which will show that the leg which gives marked clinical manifestations and is more recently affected is the more profoundly implicated in the vascular occlusion. So also in the following patient:

P. A. had four years of indefinite symptoms of rheumatism and pain in the ankle, worse in cold weather. After a trauma of the dorsum of the right foot, an ulcer formed which refused to heal. Somewhat later another ulcer appeared near the base of the little toe of the same foot.

Physical examination showed the typical involvement of the right leg, erythromelia, ischemia, absent pulsation of the posterior tibial, popliteal and dorsalis pedis arteries.

After a period of observation of about one month, edema developed and finally amputation became necessary, a Gritti being done with a successful result.

While in the hospital it was also seen that the *left leg was involved in the same process, although the patient did not know of this*, the signs being marked reactionary erythromelia, slight ischemia and absence of pulsation in the dorsalis pedis, popliteal and posterior tibial arteries.

7. *Cases with Intermittent Claudication Only.*—These are the patients who are apt to consult the orthopedist and run the gamut of mechanical appliances for an affection in which the vessels are at fault. Careful physical examination should elicit, in addition to pulseless vessels, some ischemia on elevation, either chronic or at least reactionary rubor with other signs.

Or, *closed vessels and intermittent claudication* may make up the complex for years, but sooner or later ischemia and rubor are apt to develop, and then the trophic lesion. As illustrated in one of the cases (I. M.) intermittent claudication was the chief symptom for four years, with absent pulsation of the dorsalis pedis and posterior tibial of the left leg, without erythromelia or ischemia.

Or, after a period of intermittent claudication, the other phenomena appear, many years being required for gangrene to set in.

M. L., aged 32, Russian Hebrew, examined on December 12, 1914. After about one year of intermittent claudication the left leg showed marked redness, ischemia on elevation, absence of dorsalis pedis, posterior tibial and popliteal pulsations, *without any trophic disorders*. At the same time, the right leg was also involved, the main symptoms being coldness of the big toe, cyanosis, absence of the dorsalis pedis and posterior tibial pulsations *without any other symptoms*.

8. *Cases with Intermittent Claudication and Migrating Phlebitis Only.*—Here the patient consults us for the pain on walking, the phlebitis not being complained of, but a history of such is elicited on questioning.

D., January 29, 1915, aged 20, Russian Hebrew, began five years previously with pain in the right calf and sole on walking. One year later he had migrating phlebitis along the inner side of the right thigh; none since. For six months the left foot has been affected with intermittent claudication, but not so severely as the right. No migrating phlebitis in the left leg, no history of trophic disturbance.

Physical examination. In the horizontal position both feet look fairly normal; no further evidence of phlebitis. Both femorals pulsate, the left posterior tibial pulsates, the right does not. The right dorsalis pedis is absent, the left present. In the pendent position erythromelia appears slowly but with moderate intensity over the whole of the right foot and lower leg. No evidences of trophic disorder. In this position the blanching comes on rapidly over the toes and the dorsum of the left foot. The ischemia in the left foot, however, is only moderate, for, on pressure it is seen that some blood reaches the toes. On elevation, after depression, the toes of the left foot lose the red rapidly, but develop only slight ischemia. In the right leg, however, there is more ischemia, but not marked.

Summary.—This is a case in which the right limb alone was affected, the symptom of intermittent claudication dominating, migrating phlebitis having been present. After four years there was subjectively only intermittent claudication, objectively, marked erythromelia, absent dorsalis pedis, posterior tibial, slight ischemia, and no trophic disturbances. Here was a very slowly progressing case with only slightly marked symptoms.

9. *Cases Losing the Limb Last Affected.*—Not infrequently the leg last affected will be the first to require amputation. Among numerous instances may be mentioned the following case.

A. P., with typical symptoms involving the right foot which began in May, 1906, with a burning sensation on walking, would frequently have to go into a neighboring park on his way home to take off his shoe and investigate the cause of the pain. Then, during the winter months came the feeling of coldness and soon a dark bluish black spot developed over the base of the fifth toe. Finally, ten months after the onset of the trouble, and after cutting a callus in the painful region, a sore developed which refused to heal. He was admitted to the Mt. Sinai Hospital in April, 1907, where it was found that he had a trophic ulcer on the outer border of the right foot near the head of the fifth metatarsal bone. There were also the usual typical symptoms, ischemia on elevation and rubor in the dependent position, the dorsalis pedis and posterior tibial arteries being pulseless.

In two months, however, the ulcer had healed and from *then on the foot gave him no more trouble.*

In the meantime, however, the typical symptoms of thrombo-angiitis obliterans developed *in the other leg, leading finally to amputation* during the following year.

Not infrequently the disease exists in one of the limbs for months or years without the knowledge of the patient, and is only discovered when symptoms referable to the second leg are noticed by him. In such cases the process is either developed insidiously or manifests itself simply by the presence of intermittent claudication or difficulty in walking, finally coming to a standstill without the development of trophic disturbances or gangrene. In the meantime the other limb is affected by more severe manifestations, ulceration and finally gangrene.

Such a case was J. G., aged 39, Austrian Hebrew who was seen November, 1908. Some fifteen years ago he had been troubled with weakness of the legs and thighs on walking and standing, also with indefinite pains which were only relieved by rest. These were severe enough to incapacitate him for one year. He was apparently well until three months ago, when a similar affection involved the right leg and then the foot became noticeably red in the dependent position. Soon after an ulcer developed on the dorsum of the right foot near the root of the fourth and fifth toes, which healed spontaneously, and then another ulcer appeared on the right fifth toe.

The physical examination in February, 1909, revealed evidences of involvement of both legs. The popliteal, dorsalis pedis and posterior tibial pulses of the right leg were absent, and on the left the posterior tibial and dorsalis pedis were also negative. The right foot was somewhat enlarged, tumefied, all the toes slightly thickened, a patch of gangrene being observed on the outer aspect of the fifth toe; marked erythromelia, in the dependent position, marked blanching on elevation. The left leg showed intense ischemia on elevation,

and upon depressing the leg after preliminary elevation marked compensatory erythromelia most striking over the dorsum was noticed.

In short, we have here a case in which, except for the history of some indefinite pain and intermittent claudication fifteen years previously, nothing referable to the left leg could be elicited, although ischemia, erythromelia, and absent pulsation were distinct evidences of the presence of the disease in this limb.

On March 25th the right leg was amputated because of gangrene, the left leg having in the interim again developed more active symptoms in the form of marked redness and pain.

This was, therefore, a case of insidious development of the disease in one leg and its spontaneous cure, the trouble lighting up in the other and leading to gangrene of the limb.

10. *Cases with Chronic Course in One Limb, Acute Course in the Other.* The following is a typical example.

H. R., after having exposed both feet to cold suffered from "cramps" in both legs which disappeared in a day or two (1897). A year later there was a recurrence of the pain. These indefinite pains persisted for several years, until, in 1902 the typical symptoms of intermittent claudication in the right leg came on, leading him to try various methods of treatment, but without avail. Finally, about five years after the onset of the disease, prodromal symptoms of gangrene or of trophic disturbances developed in the big toe of the right foot, the toe becoming swollen and red, and trophic disorders showed themselves under the nail, which was removed, leaving an angry red nail-bed which refused to heal. About the same time the second toe also became affected in a similar way. In 1903 the toes were still sore, but healed after several months of treatment. Then, after a period of remission of three years (1906), trophic disorders developed again in the same place, namely, the big toe of the right foot, the pain became very severe, and finally *gangrene* spread rapidly over all the toes necessitating amputation.

In short, after a period of some nine years, initiated by pain referable probably to the deep thrombosis, followed by intermittent claudication and trophic disturbances, gangrene finally set in. It is noteworthy, however, *that several years elapsed between the first attack of trophic disorders and the final onset of gangrene.*

History of the Left Leg.—In 1909 intermittent claudication of the leg, then pain and swelling of the toes, bluish discoloration of their tips, the development of superficial ulceration of the skin over the anterior part of the dorsum of the foot, gangrene of the fourth and big toes, and marked edema of the foot.

In short, a rather acute case of eight weeks' duration.

11. *Relapsing cases* may show vessels in which corresponding exacerbations are found in the deep vessels, namely, more recent thromboses and even "acute lesions" in the daughter or canalizing vessels. As a rule the free intervals are shorter than in the following case.

A. L. presented a slow clinical course, there being a seven years' history in a man 45 years of age, with sudden onset of cramps in both legs, particularly the right, apparently followed by cure of the left leg, there remaining at the time of examination only the absence of posterior tibial pulsation on the left side as evidence of previous trouble.

After a period of seven years in which intermittent claudication was the chief symptom, erythromelia and ischemia in the elevated position were to be elicited, absence of pulsation in the posterior tibial and dorsalis pedis arteries, and marked diminution of the angle of circulatory sufficiency. Then followed cyanotic discoloration of the big toe and gangrene.

Similarly, as evidencing the relapsing nature of the malady may be mentioned the following.

S. M. began with pain and coldness in the right big toe with blue discoloration in 1910, and trouble with the second toe lasting from April, 1910, to September, 1912, at the age of

25, with complete recovery. Now (1913) *recurrence* of trouble in the big toe of the right foot, swelling and gradual development of gangrene in the lower part of the thigh (total duration about three years), leading to amputation August 21, 1913.

12. *Cases with Lethal Outcome.*—So extensive may the process be, that all the extremities are involved. An *atrophic* condition of the *upper extremities* may ensue from obliteration of the *brachial artery*.

I. L., male, aged 35, Russian Hebrew, in October, 1906, began with intense pain in the left ankle. In September, 1906, an ulcer on the dorsum of the foot was followed by progressive gangrene requiring amputation October, 1906. Symptoms then developed in the right leg which became markedly ischemic and extremely painful, *so that the patient begged for amputation* which was done July 1, 1907, through the middle of the right leg. Neither stump healed well, requiring reamputation, there being continued trophic ulcers over the stumps of both legs in 1909. On December 17, 1909, there was involvement of the right hand, namely marked symptoms of scleroderma or sclerodactyly, atrophic fingers, with the brachial artery palpable as a hard cord.

On April 25, 1911, the patient was readmitted to the hospital, and the left lower extremity was again amputated because of failure to heal. On May 25, the patient became lethargic, drowsy, unable to answer questions, and ceased on May 30, 1911.¹

In short, this is a case in which both legs were amputated, the right upper extremity showing symptoms of scleroderma, marked atrophy, leading to a lethal outcome within a period of about five and one-half years.

13. *Cases in the Young with Grave Prognosis.*—Just why the disease when it affects young men under the age of twenty-five should be apt to take a very destructive course is difficult to explain. Many of the cases in the author's experience have lost one or both lower limbs within a very short time.

H. K., male, aged 27, Russian Hebrew, had been suffering since the age of *seventeen* with pain in the left foot. In 1905 trophic disturbances appeared so that early in 1906 amputation became necessary, the leg being amputated five inches below the knee. Then in 1906 symptoms developed in the right leg, pain in the foot and in the big toe which persisted up to the present time.

Physical examination April 2, 1908, showed a non-healed left stump with necrosis of the bone; typical symptoms in the right leg, marked ischemia on elevation, erythromelia, absent dorsalis pedis and posterior tibial, and trophic disorder of the big toe. On April 15, the big toe was amputated, failed to heal, but amputation was refused.

So, also, is the following case—one of a youth in whom one would expect collateral circulation to become established.

C. H., American, male, aged 25, had had vague symptoms for some years. Then coldness of the left leg, and four or five months thereafter, discoloration of the forepart of the left foot were noted. The heel, the big and fifth toes were painful, and trophic disturbances of these toes with gangrene developed after about one and one-half years of definite symptoms. The dorsalis pedis, posterior tibial and popliteal arteries of the left leg were pulseless, as also the dorsalis pedis of the right leg.

Finally, in January, 1910, amputation took place. This was done eight inches below the knee with a poor result, suppuration continuing, due to necrosis of the bone.

In short, within a period of two years both legs were affected in a boy twenty-five years of age, leading to amputation of the left leg, the process having been only slightly advanced in the right.

14. *Cases of Long Duration without Trophic Lesions.*—Because so many years may elapse without manifestations of nutritive derangement of the distal parts, the clinical picture devoid of this symptom should be recognized. The author's records show instances where eight to ten, and even *fifteen years* had passed without ulceration or gangrene. The following case may be cited.

B. H., Russian Hebrew, male, aged 47, seen October 19, 1910, began eight years ago with pain on walking, intermittent claudication, one year later manifestations of migrating

¹ This case because of its importance is discussed more fully on p. 372.

phlebitis, and for about one year the feet have been cold. Six years ago he noticed discoloration of the feet.

On physical examination both feet were found to be involved with the typical symptoms, erythromelia and ischemia, the left being more marked both as regards erythromelia and ischemia, than the right. On the right, the dorsalis pedis and posterior tibial were pulseless; on the left, pulsation was absent in these vessels as well as in the popliteal.

Here is a case of long standing in which the trouble dated back farther than the history would indicate, with involvement of both legs after an eight years' course, with development of all the typical symptoms up to the stage in which ulceration was imminent.

15. *Cases with All Extremities Involved.*—Not unusual is it to note that both upper extremities may participate in the process, although the destructive force of the vascular occlusion makes itself but slightly felt in the upper limbs (Chap. LIX).

M. F., Russian Hebrew, aged 34, began at the age of thirty with pain in the right foot. This was followed by numbness of the right hand. Six months ago symptoms were observed in the left foot, such as coldness and pain on walking.

On physical examination it was found that the right hand and left leg were distinctly involved, there being atrophy of the right hand and coldness of the fingers with a faint radial pulse. The left foot showed evidences of involvement, rubor, coldness and absent dorsalis pedis and posterior tibial.

Five years after the onset of symptoms in the left leg, the second toe became gangrenous. The foot was in a state of marked erythromelia, and the pulsations in the posterior and anterior tibial arteries were absent. Gritti-Stokes amputation was done with good result.

Eighteen months after the amputation of the left leg, the patient complained of intense pain in the calf of the right leg accompanied by the formation of an ulcer on the foot. The symptoms progressed and conservative amputation was done below the knee. However, owing to the persistence of an ulcer on the right stump for 6 months, Gritti-Stokes amputation was finally resorted to with complete abatement of all the symptoms.

Two years after the last amputation the patient gave evidences of involvement of the left upper extremity, in the presence of pain and coldness of that part. The left radial pulse was found imperceptible, the right barely palpable.

When last seen (September 8, 1922) the patient, who has been addicted to morphine was free of all symptoms, the left radial pulse, however, being imperceptible.

16. *Cases with Pain Only.*—Recognition depending on objective signs are amongst those usually undiagnosed. There are no trophic disorders. The patients usually have been treated by an orthopedist, but the ischemia, rubor and pulseless vessels should direct attention to the true nature of the malady.

M. N., Russian Hebrew, aged 35, presented a picture of thrombo-angiitis obliterans without trophic disturbances, simply marked ischemia, moderate erythromelia after a period of indefinite pain which had been diagnosed as due to flat foot. The arteries of both legs failed to pulsate.

17. *Cases without Trophic Disorder or Gangrene Requiring Amputation.*—There have been a number of cases in our experience, either with one or both limbs affected, that suffered such agonizing pain for an extended period of time, that they vehemently begged for amputation, which was carried out in several instances. The following may be cited as an example.

H. R., August 6, 1916, born in the United States, Hebrew, began to experience pain 16 months previously in the calf of the left leg, the pain extending downward over the entire leg and foot, especially over the toes. The pain was severe, cramp-like in character, intensified by walking, diagnosed as due to flat feet. There was a history of migrating phlebitis of both lower extremities a year previously.

Physical examination, August 6, 1916. The left foot was markedly cold and somewhat smaller (atrophic) than the right, and in a state of chronic rubor, most marked in the pendent position. On elevation there was intense pallor, on depression marked congestion

erythromelia, and rubor. None of the pulses, neither the dorsalis pedis nor posterior tibial arteries were palpable.

Diagnosis.—Thrombo-angiitis obliterans without trophic disorder or gangrene.

The patient was kept under observation for some 12 days, and his supplication to have the limb removed was finally acceded to.

At operation, August 18, 1916, amputation of the left leg (Gritti-Stokes), most of the arteries were found closed, the popliteal also being filled with organized thrombus. The popliteal veins were open.

18. *Cases with All the Vessels Pulsating.*—These will be described in more detail under Borderline Cases (Chap. CIV). Clinical and pathological investigations have demonstrated that an atypical clinical picture with predominating vasomotor symptoms, or even the typical picture of thrombo-angiitis obliterans may be produced, when the vascular lesions are confined to the territory of the plantar or the digital vessels, with occasional involvements of the distal parts of the dorsalis hallucis. The symptoms may begin with vague pains in the feet to which little attention is paid, or coldness of the toes. Later on this pain becomes severe, is referred to one or more toes, and is followed by cyanosis or rubor, or a combination of both. Or, the pain may be slight, and the coldness and cyanotic discoloration may be noteworthy. In the latter case the clinical picture may simulate that of some of the vasomotor neuroses. When pain is marked, a diagnosis of incipient or restricted vascular occlusion can be made with a fair degree of certainty.

M. C., Russian Hebrew, consulted me on the 7th of July, 1911. He was devoid of symptoms until 2 weeks previously, when he suddenly began to experience pain in the whole left foot. At first the pain was slight, but became gradually more and more severe. After a week the toes became red without being preceded by any ischemia. Since then the third toe has become blackish and ulcerated, and now the pain is intense by day and night.

Physical Examination.—Left foot shows discoloration of the third, fourth and fifth toes, these being cyanotic. The fourth toe is reddened. On the inner side of the tip of the middle toe there is a patch of superficial gangrene of the skin about the size of a ten cent piece, the center being ulcerated. The tip of the toe is very cyanotic, suggestive of impending gangrene. On elevation of the foot the visible veins become empty, the third, fourth and fifth toes slightly bluish, but no distinct blanching can be elicited.

All of the vessels of both extremities pulsate normally.

Conclusion: Although an absolute positive diagnosis could not be made in this case, since amputation was not done, a number of other similar cases have shown conclusively that the clinical picture represented occlusive thrombo-angiitis obliterans confined to the territory of the plantar and digital arteries.

19. *Cases with Marked Involvement of the Upper Extremities* are discussed in full elsewhere (Chap. LIX).

20. *Cases with Migrating Phlebitis* are of such importance as to warrant special consideration later on (Chap. LVIII).

21. *Cases in Females.*—So rare is the disease in females, that doubt has been cast on the possibility of its occurrence outside of the male sex. The author has observed but 3 cases that were clinically indistinguishable from typical thrombo-angiitis obliterans, but since amputation did not become necessary in any of them, pathological confirmation is missing.

Raynaud's syndrome in elderly women with arteriosclerotic vessels or acrocyanosis may give confusing clinical combinations, that should be carefully differentiated from thrombo-angiitis obliterans.

A case that belongs clinically to thrombo-angiitis is the following.

M. D., female, American, seen February 2, 1912, parents Bavarian Jews, was always perfectly well except for "sciatica" in October, 1911, possibly related to her present trouble. About this time she had an attack of pain in the right thigh and foot which was so severe

that she was kept in bed for two weeks. The diagnosis was "sciatica" from which she apparently recovered, but discomfort and even pain remained in the right sole and instep. The right foot, too, seemed much colder than the left, not bluish but pale at times, always appearing whiter than the left foot. After walking about one block, the pain would become so intense that she had to stop and rest.

In short, an indefinite history of sciatica followed by pain in the foot, coldness, pallor and intermittent claudication.

Physical examination, February 2, 1912, revealed the absence of the dorsalis pedis pulse of the right foot, a doubtful posterior tibial, all the other vessels of both sides pulsating. On elevation the right foot showed moderate ischemia. Examination of the sensory nerve condition was negative.

Diagnosis: A case of thrombo-angiitis obliterans with moderate erythromelia of the right foot in the dependent position, ischemia on elevation, absent dorsalis pedis with a history of pain in the foot, ankle and sole following sciatica.

The patient was not seen again until some four months later, when in June, 1912, the following history was taken. Since the last examination she had been receiving hot air treatment, which she believed caused a burn. An ulcer developed under the big toenail of the right foot, the nail subsequently falling off. The nail-bed healed after four weeks. About February 16, the foot became very bad, the toes looked almost black, so that in March after several consultations with surgeons amputation was advised. The big toe particularly seemed affected being bluish black, the bed of the nail having become gangrenous. Certain ointments were used, the symptoms gradually subsided, amputation was refused, and healing took place.

June 19, 1912, physical examination of the right leg in the horizontal position showed cyanosis of the big toe, with a deformed nail. There was slight erythromelia of the forepart of the foot in the dependent position, marked ischemia on elevation, especially over the sole, less over the dorsum of the foot. A fairly marked reactionary erythromelia was produced when the foot was returned to the horizontal, and absence of pulsation of the dorsalis pedis and posterior tibial arteries was noted.

In short, since the last examination the patient developed trophic disorders which were probably not at all related to the hot air treatment, and might have come on spontaneously; erythromelia had become more marked, as also ischemia, and the dorsalis pedis and posterior tibial were definitely occluded.

The patient was again seen on January 4, 1913, when both feet were slightly cold without evidences of atrophy. In the pendent position the right foot showed definite rubor. On elevation both feet showed *distinct blanching and there was distinct reactionary erythromelia of the right leg after elevation*. The dorsalis pedis and posterior tibial arteries of the right were not palpable, as well as the dorsalis pedis of the left foot.

Summary: January, 1913, although the process had not progressed much in the right leg, *the left leg also* seemed now to be involved.

June 10, 1913, the patient said the right foot had become distinctly warmer, and she considered herself much improved being able to get about much better. Physical examination showed the same condition of the pulses as at the last examination. The right foot showed marked erythromelia, the left but slight, both evidencing distinct ischemia on elevation.

The following case may be cited as another example of thrombo-angiitis obliterans in a female.

A. C., 38 years of age, began with pain in the calf of the right leg upon walking following an attack of influenza 2 years ago. The right leg became swollen, but after 6 months the cramps in the calf disappeared, the swelling, however, persisting accompanied by numbness of all the toes. Eight months ago the right foot became cold, and the patient noticed a red spot on the inner aspect of the right leg.

Physical examination reveals edema of the right foot and leg, more marked over the ankle. The great toe is hemorrhagic, showing evidences of discoloration of the tip with ecchymosis. There is moderate erythromelia over the forepart of the right foot. Elevation elicits considerable ischemia. Upon return to the horizontal position, the color does not return for some time, rubor appearing first above the roots of the toes, the toes themselves remaining ischemic and cyanotic.

The dorsalis pedis and posterior tibial pulses of the right foot are absent, those of the left present.

In short, thrombo-angiitis obliterans in a female, with involvement of the right lower extremity, the chief symptoms being erythromelia, ischemia and absent pulsations.

22. *Cases in Elderly Individuals* will offer difficulty in differentiation from sclerotic vascular diseases all the more so since the two conditions may co-exist simultaneously, the latter usually engrafted upon the former when in the silent, latent, or anatomically "healed" stage. Autopsy findings (Chap. LXIII) have convinced the author that the arteries are particularly prone to lesions of atherosclerosis, although the territories involved with thrombo-angiitis obliterans may be least or not at all affected.

There is a series of cases in which the symptoms apparently become severe after the age of forty. In these, a careful search into the history will reveal the fact that there had been symptoms many years previously, and in all probability the disease had come to a standstill. Therefore, in view of this fact we must give a rather guarded prognosis in all cases of thrombo-angiitis obliterans that apparently heal. Our experience with cases in young men between twenty-five and forty years in whom complete cessation of all manifestations takes place, confirms the diagnostic assumption of the previous existence of the disease in some of the older arteriosclerotic individuals.

Pathological pictures afford the anatomic corroboration for the coincidental occurrence of the two affections.

23. *Cases with Apparent Healing or "Cure."*—Clinical inactivity, abatement of pain and intermittent claudication, improvement in ability to walk and the absence of trophic lesions are interpreted by the patient as indicating subsidence of the disease, usually in the words "my legs give me no more trouble." That such a free interval is to be regarded under all circumstances as of doubtful duration, experience has taught. An interruption by a repetition of the manifestations in the other limb is not uncommon as elsewhere described.

In the period of clinical inactivity, however, the existence of the disease should not escape our observation, since slight ischemia, or some rubor or reactionary rubor, or a diminished angle of circulatory sufficiency and pulseless vessels can be demonstrated, these signs in varying combinations and degree of intensity.

One of the most exquisite examples of apparently complete clinical cure of a case in which trophic disorders had been present, and imminent gangrene of one limb had impelled a surgeon to advise amputation, is afforded by the following case.

J. R., Russian Hebrew, aged 32, consulted the author September 9, 1909 to ascertain his condition, since his brother had the same disease and was developing gangrene. In 1894 (at the age of seventeen) he began to experience a peculiar cutting pain in the left calf on walking a short distance, so that he had to drag the limb. This symptom (probably intermittent claudication) persisted for about two years during which time he often could not sleep at night because of the pain and burning in the toes. In 1896 the case was diagnosticated as *erythromelalgia*, for at that time his leg was very red. *The right leg, on the other hand, at no time gave him any symptoms.* Another surgeon about this time made the diagnosis of flat foot and put the foot in a cast for two weeks. After the cast was taken off, a sore developed on the inner side of the left ankle which refused to heal (decubitus?). In spite of all the measures taken to bring about the healing of this ulcer, the wound was still open one year after the removal of the cast. At that time, the symptoms were so intense that he was advised to have the *limb amputated*, but refused, and a year later the wound spontaneously closed with the use of ichthyol dressing, and gradually after this time (1898), four years after the onset, *all the symptoms left him, and he has been free from trouble ever since.*

September 11, 1909, one year after the wound closed, he was examined by the author, and *all the vessels of both lower extremities, including the femorals, popliteals, posterior tibials and dorsalis pedes were found pulseless.* Both feet showed a very slight rubor in the pendent position, but not of sufficient amount to be diagnosticated as erythromelia. Besides this, there was *distinct ischemia* in the elevated position, but not at all marked. There were *no*

trophic disturbances, the patient complained of no pain, and considered himself perfectly well. There was no intermittent claudication, nor any symptoms referable to the lower extremities.

In short, we have here a case of typical thrombo-angiitis obliterans in the left limb, spontaneously "cured" as far as symptoms are concerned, in spite of the fact that extensive obliteration of vessels had occurred. There seems to be no question but that the disease must have been present in the right limb also, *although at no time did the patient discover any symptoms*.

The following history is suggestive of the presence of lesions in one limb, that however, spontaneously healed.

A. L. gave a history of cramps in the left leg as well as in the right, and on examination seven years later marked symptoms of thrombo-angiitis were found in the right leg. In the left, the only symptoms of the disease were the absence of pulsation of the posterior tibial and at times *cyanosis* of the big toe in the dependent position. Therefore, all the symptoms had subsided, these two signs being the only ones left indicative of previous trouble.

Some cases may go along for a year with the development of gangrene of one toe and trophic disturbances, as well as all the usual symptoms, and then spontaneously after hot air or postural treatment show complete subsidence of all symptoms. Such a case was the following.

H. G. developed gangrene of the big toe after a year of the usual pains and intermittent claudication (December, 1910). This gradually healed while he was treated in January, 1911, by the hot air method, and remained perfectly well under our observation for four years, so that when the patient was seen in December, 1914, the left foot, although presenting a somewhat atrophic appearance, an absent dorsalis pedis and posterior tibial pulse, was found otherwise in fairly good condition as far as circulation was concerned, and presented no symptoms whatever.

Some of our cases were observed for several years, and although at times there was slight exacerbation, many of them showed no tendency to marked progression or to the development of gangrene, so that they could be regarded as stationary or clinically "cured." As,

A. G., was observed from November 27, 1908 to May 9, 1911. He had had a typical history of intermittent claudication of the left leg, followed after two years by pain in the region of a trophic lesion. This spontaneously healed, and when the patient was seen in 1908 there were definite evidences of involvement of both legs with a history of pain on walking, coldness of the foot, thin condition of the foot, and numbness with occasional whitening or pallor of the foot on walking. Although the patient was seen and carefully examined some four or five times a year, no aggravation of his condition was noted, no ulcers developed, and the case was regarded in 1911 as being a *stationary* one, the cyanosis, the pulseless vessels, the tendency to coldness and numbness of the feet persisting.

In short, we have here a proof of the fact that six years may elapse without any marked destruction of parts, and without gangrene.

24. *Arrested Stage or Temporary Healing in Thrombo-angiitis Obliterans.* Surprising changes both for the worse and for the better are the impressive features of the variegated clinical picture of thrombo-angiitis obliterans. So, we occasionally are confronted with a stage of threatening gangrene of the leg which limits itself and becomes restricted to the disintegration of but a part of a phalanx or less. Or, one may observe the complex—*ischemia*, *rubor*, pain and trophic disorders—all disappear with its subjective symptoms, the patient believing himself cured as far as the previously affected limb is concerned. When we encounter such cases during a period of renewed morbid activities in the other extremity, the residual diagnostic features such as atrophy and pulseless vessels can be appreciated and given deserved consideration. Periods of remission, arrest of symptoms with either none or very slight manifestations may last for years, but the possibility

and probability of an exacerbation leading to eventual loss of the limb must be borne in mind, since such an issue is extremely common.

A good illustration of such subsidence and practically complete abatement of circulatory disturbances is worthy of attentive contemplation to aid in both diagnostic and prognostic conception of the malady. So we will cite the case of

Typical thrombo-angiitis obliterans of the left leg, gangrene of toe, "healing" or arrest and disappearance of symptoms, followed by involvement of the right leg, four years after cessation, relapse and extension of lesion in the left leg.

H. G., male, Hebrew (born in Turkey) age 39 years, examined December 10, 1910, smoked fifteen Turkish cigarettes a day beginning at the age of fifteen. The diagnosis of flat feet was made ten months ago when he had pain in the left calf, also the diagnosis of "rheumatism." He then used plates for the left foot. There was pain in the left calf on walking three to four blocks. No history of migrating phlebitis could be elicited, and the right leg was free of symptoms.

Five weeks ago there was pain in the left big toe, and four weeks ago redness. For the past week a black spot had been seen on the outer side of the left big toe. Now the patient has most pain in the big and second toes, particularly at night, sleeping only a couple of hours.

Physical Examination.—December 10, 1910, the left foot is in a state of chronic erythromelia, and the big toe shows a dry gangrenous patch on the outer side 1 cm. in diameter, the rest of it being cyanotic.

The iliac, femoral and popliteal arteries of both legs were found pulsating, the posterior tibial and dorsalis pedis pulses of the right leg palpable, those of the left not.

There was a moderate increase of the erythromelia in the pendent, moderate ischemia in the elevated position.

On January 1, 1911, there was still an ulcer about one-half inch in diameter on the big toe.

On March 14, 1914 the following history was obtained. Since early in 1911 the *left* leg had given him no more concern, and since the healing of the ulcer, all symptoms vanished. For two months, however, the *right* leg had been troubling him with a sensation of pins in the sole of the foot, so that he had to rest at every block, and when he walked the pain ascended into the right calf. The right foot, too, had been discolored in the forepart.

Physical Examination (March, 1914).—The right foot is bluish red, the toes being most involved. The dorsalis pedis and posterior tibial do not pulsate, the femoral does. The *left* foot, which is now without symptoms, has a somewhat atrophic appearance, but is negative except for the absent dorsalis pedis and posterior tibial pulses.

On elevation it is very evident that the circulation *of the right foot is worse than that of the left*. This can be seen particularly over the sole, where the right foot takes on a greenish white appearance with the small toe cyanotic. If we press the other toes, those of the right foot show very little blood, and that which is present is of a purplish tint, whereas on pressing the toes of the left foot, considerable red color is in evidence. During the period of elevation even the dorsum of the right foot became markedly blanched.

On putting the foot back in the horizontal position, the return of color is seen as a mottling over the right foot, the toes being the last to regain their color.

In the pendent position the return of blood in the right foot makes it intensely red, the rubor extending somewhat above the ankle.

In short, four years after our first observation, the left foot was found (March 14, 1914) in an arrested or temporarily healed state, the right previously normal, then actively implicated in the disease.

October 27, 1914, the right foot has the intense red look and the puffy appearance of the old chronic cases. In the pendent position, the erythromelia deepens rapidly and then cyanosis comes on. The fourth toe, the distal phalanx of which is already separated, shows a gangrenous area of skin. The fifth toe is completely absent and the foot is very cold. The pain seems to be relieved in the pendent position.

When again seen on January 15, 1915, these notes were taken. The patient feels better now, but still has intermittent claudication in the left leg, and pain between the third and fourth toes of the right foot, where there is a patch of gangrene.

Both feet are in a state of chronic erythromelia, the right more marked than the left. The right foot is somewhat enlarged, the toes slightly swollen, so also the dorsum. Where the fifth toe spontaneously separated, the wound has healed. The site of the separation of the terminal phalanges of the fourth toe of the right foot still shows a dry smooth patch. In the *horizontal position* there is practically no erythromelia of the left foot, and only slight of the right, but in the *pendent position* both feet show fairly marked erythromelia. It is

noteworthy that the left foot shows this erythromelia although there are no trophic disturbances. The dorsalis pedis and posterior tibial of both feet are pulseless. He has no pain when at rest. On elevation there is marked blanching of the left foot, slight of the right.

In brief, four years after establishment of the quiescent stage in the left foot, a fresh exacerbation with recurrence of erythromelia, ischemia and pain.

25. *Doubtful Cases.*¹—Such a group is but a clinical and arbitrary segregation of cases, the exact nature of which may seem questionable, at least during a part of their clinical course. Because of the absence of pathognomonic symptoms during the early stages of certain cases of thrombo-angiitis obliterans, and because of the association of vasomotor symptoms in others, enough data for any other than a presumptive diagnosis may fail to be at hand.

To divorce the following clinical complex altogether from thrombo-angiitis obliterans and to make a symptomatic diagnosis of intermittent claudication as has been done by Erb and others, would be tantamount to a relinquishment of every desire to aim at a pathologic differentiation. Confronted with a case of cramps or pain in the legs or feet on walking, without static cause, without any history of migrating phlebitis, without either ischemia, rubor or pulseless vessels, we may be allowed to suspect that thrombo-angiitis obliterans is developing, and that it has as yet affected none other than those arteries that are beyond the reach of palpation—*e.g.* the distal branches of the anterior tibial and the plantars. To extend the designation of intermittent claudication so as to denote a possible clinical and pathological entity, would be subversive of all modern attempts to clarify clinical concepts. For, intermittent claudication, as has been elsewhere lucidated, should be restricted so as to indicate coordinate manifestations; that is, a “symptomatic association,” and not a “symptom complex,” when the latter appellation is used as the equivalent of a morbid unity. So we may allow such patients to constitute a group entitled “Thrombo-angiitis obliterans with latent (*larvata*) or undeveloped physical signs.”

This variety must not be confounded with that already alluded to, in which a patient is unaware of the disease, that is, “Thrombo-angiitis obliterans without subjective symptoms.” For, in the latter no complaint is made, whilst amongst the instances belonging here, the patient’s discomfort may be great. It is merely an insufficiency of pathognomonic objective signs that warrants this classification.

Amongst the various cases encountered are the following:

- (a) Intermittent claudication only with absolutely no objective signs;
- (b) Coldness and cyanosis of the toes, possibly with local pain; but the physical signs of thrombo-angiitis obliterans absent.

CHAPTER XLIII

THROMBO-ANGIITIS OBLITERANS—CLINICAL PICTURE

Classification.—For purposes of clinical diagnosis it is useful to divide the cases of thrombo-angiitis obliterans into four groups.

- I. Typical thrombo-angiitis obliterans of the lower extremities.

¹ Vide also Chap. CIV.

II. Thrombo-angiitis obliterans with associated thrombo-phlebitis or migrating phlebitis.

III. Thrombo-angiitis obliterans with involvement of the upper extremities.

IV. Thrombo-angiitis obliterans with secondary or complicating athero- or arteriosclerosis.

It must be remembered, however, that this grouping is artificial, for many cases may belong to one or more of these subdivisions at the same time. Thus, cases in group I may be affected with migrating phlebitis, or may have symptoms of thrombo-angiitis obliterans of the upper extremities. The classification is helpful for description and study.

For purposes of treatment it is often useful to divide the cases according to the stage of the development of symptoms at the time of clinical observation, into

1. The prodromal stage, that of intermittent claudication (sometimes with migrating phlebitis).

2. The stage of trophic disorders and gangrene.

I. TYPICAL THROMBO-ANGIITIS OBLITERANS OF THE LOWER EXTREMITIES.—The clinical picture varies considerably, depending upon the duration of the disease when the patient is examined, the severity, the effects of exposure, traumatism and complications. The following case types may facilitate the recognition of the disease, although they must not be considered as exhaustive. They should be recognized, since they are in most instances but the prodromal manifestations of gangrene.

A brief exposition of some of the typical forms of onset (A) of the malady in the lower extremities, and short summaries of some of the more usual clinical pictures (B) as they are developed under our observation, may serve to clarify our concepts of the effects of the morbid lesions in the vessels.

A. Forms of Onset. 1. *Onset with Intermittent Claudication.*—This symptom-complex need not be discussed in detail since it has been described elsewhere.¹ But allusion may be made to its importance as one of the first manifestations of the disease. Very frequently it antedates by weeks, months or years, the other symptoms—the rubor, the coldness, the cyanosis, the blanching, the migrating phlebitis and trophic lesions. It may succeed the attacks of phlebitis or the attacks of pain referable to the deep vessels. And, it may be regarded as of such negligible character by the patient, as to escape his notice, whenever more serious phenomena such as ulcers and exquisite local pain in a toe render it comparatively insignificant. On the whole, it is a sign of such distinctive character, as to be regarded as an important and integral part of the clinical picture.

2. *Onset with Symptoms Referable to the Deep Vessels (Acute Stage).*—In a number of cases there is a history of a rather sudden onset, with attacks of severe pain in the calf of one of the legs, without demonstrable cause, and attributed by the patient either to exposure to cold, or to severe exercises, or, described as coming on without reason. In a number of such cases symptoms of intermittent claudication developed somewhat later, but the history of acute symptoms was so definite, that it seemed reasonable to conclude that they bore some relation to the occurrence of thrombosis in the deep vessels (Chap. XLI, p. 219).

Quite a number of cases describe the onset as being sudden, with pain in the calf and foot made worse by walking. After a time, the acute symptoms

¹ Chap. XXVI.

give way to a recurring cramp or pain of moderate severity brought on by walking (intermittent claudication). It is more than likely that in many of these cases this acute onset marks the inflammatory stage of the disease in the deep vessels and is followed by the stage of intermittent claudication, where the pain is dependent upon circulatory deficiency.

It is quite a difficult matter in all cases to get a definite history of the onset of the disease. If the hypothesis regarding the relationship between the symptoms and the occurrence of the thrombosis of the deep vessels is correct, namely, that certain attacks of cramp-like pain in the calves and in the legs may accompany the real onset of the disease, we should be able to elicit such a history in most of the cases. However, this is not possible. If we take into consideration the type of cases with which we are dealing and the lack of intelligence of some of the patients, their failure to properly estimate and recall symptoms occurring many years back, will not be surprising.

Then, as for the symptoms which do not really belong and are really not due to the onset of the pathological lesion, we may say that these also vary in their incipency. In some of the cases there is no question but that the disease seems to begin with symptoms of intermittent claudication. In some others, however, we were unable to obtain such a history, for the patients referred their pain to the foot or to the toes, and particularly to those toes or that toe which very soon becomes the seat of trophic disorder or gangrene. In a certain case there was a history of pain in the fifth toe of the right leg at the very beginning of the disease. Two weeks later ulceration took place and at the end of the month the toe was amputated for gangrene.

If we carefully analyze such a history, we cannot doubt but that the pain complained of was that of the impending trophic disorders and gangrene. It is more than likely that other manifestations had initiated the real beginning of the disease, but had remained unnoticed.

3. *Onset Overlooked, Trophic Lesions First Noted.*—In the careless, ignorant hyposensitive individual, the first indication of trouble may be the development of an ulcer or even a patch of gangrene; or, exquisite pain in a toe, usually the forerunner of serious nutritional disturbance is the first noticeable manifestation.

Careful scrutiny of many of the histories demonstrates conclusively that the onset of the disease is often overlooked. In some cases, we find that one toe has been amputated, and in eliciting the history, we find that a sore had developed many years ago without cause, leading to spontaneous gangrene and finally amputation. Thus, in one case the history states distinctly that fifteen years previously the big toe of the left foot was amputated for spontaneous gangrene, the patient remembering no other symptom associated with it other than the local pain.

4. *Onset Overlooked until Second Leg Affected.*—In the chapter on the Course of the Disease, the latency of the affection and the insidious manner in which it may implicate one extremity, wholly unknown to the patient, have been discussed. Here, it may be permissible to emphasize merely that a medical examination should not disregard the following signs of arterial involvement in a limb, *that apparently gives the patient no concern*; namely, absent dorsalis pedis or posterior tibial pulses, with or without rubor or ischemia, and coldness of a portion of the periphery or cyanosis. When merely one pulseless vessel is the only apparent objective sign, careful search for reactionary rubor and for ischemia after repeated and prolonged elevation may be rewarded by positive findings sufficient to warrant the diagnosis.

5. *Onset with Coldness and Cyanosis.*—The symptoms to which the practitioner is wont to give too little heed are coldness and blueness of one or more toes with or without pain. It is true, other manifestations wholly ignored by the patient may precede, but it is for the signs of discomfort that the patient seeks relief. If a routine examination according to the principles laid down be followed, an early diagnosis may be made.

6. *Onset with "Rheumatic Pains."*—Pain described as such, when referred to the ankle, the foot or the tibia, and when not typical of intermittent claudication, is a symptom whose significance may be underestimated. This dictum may be safely accepted, *that in a young Hebrew, especially of Russian or Polish origin, any persistent discomfort in the foot or leg justifies careful investigation as to the integrity of the arteries of the limb, because of the manifold variations in the symptomatology.*

B. Usual Clinical Pictures.—Some of the more common clinical manifestations group themselves in our experience as follows:

1. Symptoms of intermittent claudication, namely, pain in the calf of the leg or in the foot, made worse by exercise and walking, may last for a variable period of time, and then distinct rubor or erythromelia develops, the picture being a combination of these two chief symptoms.

2. Symptoms of intermittent claudication may predominate for long periods, may remain unrecognized, but should be regarded with suspicion if they are accompanied by blanching of the foot upon elevation, rubor upon depression of the foot after elevation, and loss of pulsation in the dorsalis pedis, possibly posterior tibial, or both, or even the popliteal arteries.

3. Symptoms of pain or intermittent claudication may give way after a variable time to trophic disturbances, ulcers, fissures, hemorrhagic blebs, scaling of the skin, etc., but when these are present, the typical phenomena elicited by physical examination are regularly to be found.

4. Thrombo-angiitis obliterans may develop silently in one limb without symptoms, indefinite signs of pain, indefinite intermittent claudication having been present and having been unnoticed or undiagnosed, being only elicited when the patient seeks advice for characteristic symptoms of thrombo-angiitis obliterans in the other limb. Physical examination will reveal absence of pulses, in one or both limbs.

5. The symptoms of thrombo-angiitis obliterans may develop in an orderly and typical sequence, namely: first, stage of indefinite pains or intermittent claudication; second, stage of rubor or erythromelia, with absent pulsations, and ischemia on elevation; third, a stage of trophic disorder; finally, a stage of gangrene.

6. Cases may pass through any of these stages and the progress of the disease may become arrested spontaneously, or with treatment. Those in which the signs of intermittent claudication and pain alone have developed, will regularly show upon examination the ischemia on elevation, or at least, some reactionary erythromelia, absent pulse in at least one of the larger peripheral vessels, such as the dorsalis pedis and posterior tibial, or often both. When the disease comes to a standstill, the subjective symptoms disappear, but the objective may persist for a long time, that is, the ischemia on elevation, the absent pulses and the erythromelia. In some of these, however, even the ischemia and the reactionary erythromelia may become absent, the pulseless vessels alone remaining as indications of the disease. When erythromelia becomes marked, it is likely to persist for a long time, even after the disease is spontaneously arrested, or apparently cured by treatment.

When trophic disorders develop, the pain is wont to become severe. Ulcers may spontaneously heal; the pain may leave the patient; the intermittent claudication may abate, the ischemia and erythromelia being the last phenomena to disappear.

Those patients with gangrene who become spontaneously cured, pass through the stages indicated above, the typical phases of mortification, involving as a rule only small portions of a toe, or a toe, being followed by a long period of convalescence, lasting months or even years, and resulting finally in cure. In these, too, the pulseless vessels will tell the tale, erythromelia persisting for a long time.

7. The Chronic or Incurable Cases.—These are common, the disease in most instances being a progressive one. The advent of the various stages, although often delayed may be expected to develop. In the chronically progressive type, amputation may become necessary, either in the stages of trophic disorder, or gangrene. The pain may be so excruciating that sleep is impossible, amputation finally being the last resort, even though the lesions are merely those of ulceration with or without infection; or, the control of pain in cases of gangrene may also be impossible, amputation being the only method of obtaining relief.

8. Cases in which any of the above symptoms or complexes may affect first one lower extremity, then the other, possibly abating in the extremity first involved, and making more marked progress in the other. There are cases in which one or both lower extremities are involved, and in the further course of the disease one or both upper extremities also give manifestations of the same affection. These will be considered under the group—Thrombo-angiitis Obliterans of the Upper Extremities.

9. Fulminating Cases.—Although the regular course of the disease is a chronic, progressive one with a long prodromal period, there are cases in which (according to the histories) very rapid development of gangrene can take place. It is possible that the prodromal phenomena were unnoticed, being of slight degree, or developing insidiously. In these patients coldness of the foot and pain in the toes may be the first symptoms, leading rapidly to areas of mortification.

CHAPTER XLIV

THROMBO-ANGIITIS OBLITERANS—APPEARANCE OF THE LIMB

Since the special and more or less striking deviations in the appearance of limbs affected with thrombo-angiitis obliterans are to be described separately, there remains to be mentioned here only those general peculiarities of color and conformation that cannot be classed into single categories, but that are the result of a combination of factors, partly nutritional, partly compensatory tissue growth, partly adaptation, and partly circulatory derangement.

Leaving out of consideration, then, the appearance of the extremity when it is discolored into marked pallor (ischemia), rubor (erythromelia, hyperemia), or cyanosis (asphyxia, lividity), when changed because it harbors trophic ulcers and infections or gangrene, then there are still at hand

certain peculiarities that are the more or less characteristic products of the many factors at play in this disease.

For our diagnostic purposes, it is true, our inspection should be concentrated first and foremost on the more striking alterations above reviewed; but for special differentiation, even minor changes are of no mean import.

In the cases with but few symptoms, with pain or intermittent claudication predominating, there may be nothing worthy of note other than dystrophic alterations in the nails; or even these may be absent. When, however, rubor has existed for some time, and more particularly when trophic lesions have been or are present, the gross appearance of the foot undergoes distinct changes. These vary in intensity and extent. It is very common to not a peculiar thickening of the subcutaneous tissues that differs from edema and that corresponds to chronic lesions under the skin. Through this the normal markings as expressed by the prominence of the tendons and the intervening furrows, may become diminished or effaced. The normal displaceability and elasticity of the skin gives way to a more hide-like or leathery-like texture, whilst the cutis itself, need not necessarily appear to be thickened. The toes in the territories that have suffered most marked circulatory impoverishment may be enlarged, waxy in appearance, devoid of wrinkles or furrows, and filled out as it were, in a manner that does not yield to pressure, as does edema.

Alterations in the nails may be the sequence of trophic lesions in their immediate neighborhood, as in the healed ulcerative lesions; or the nails—especially of the fingers (Chap. LIX, p. 298) may become distorted, lifted off the matrix and opaque, whilst the matrix becomes white, the cuticle retracting so as to leave an exaggerated, enlarged, yellow white and dirty looking lunula.

Fissures over the soles, between the toes, near the margin of the nails, in and near callouses, must not escape the watchful eye. For not only do these give pain, but they may extend much deeper than we would suppose at first glance, and further, may be but the harbingers of a serious menace to the integrity of the part. For out of these, infections and gangrenous lesions are apt to develop.

Atrophic changes of the skin are more often symptomatic of the results of marked atherosclerotic disease than of thrombo-angiitis obliterans. However, in that stage of chronic pseudophthisis or atrophy of the limb that occasionally belongs here; or in some of the pseudo scleroderma lesions, or in the vicinity of amputated limbs, striking atrophy is occasionally encountered.

A peculiar mottling of the skin of the distal parts, especially over the digits seems to be the result of chronic circulatory disturbances. If one compares this mottling of the diseased with the normal foot, one can appreciate that it really represents an intensification of the normal venules, which, by virtue of stasis, become permanently dilated. The mottling is produced by streaks rather than by patches of discoloration and is brought out with greatest intensity when the limb is held up for purposes of eliciting ischemia. In some cases, hemorrhages take place with pigmentation, resulting in a permanent brownish discoloration. The skin is apt to be thin over such areas but when there is a combination of chronic enlargement of the toes, the general puffiness may be obscured by mottling.

Atrophy of the leg, more rarely of the thigh, in varying degrees, is not uncommon where the popliteal and femoral arteries have become closed. This diminution of the girth of the calf is best appreciated with the patient in the prone position, when the contrast in the size of the calf muscles is noticeable.

CHAPTER XLV

THROMBO-ANGIITIS OBLITERANS—ISCHEMIA

Ischemia, blanching or whiteness of the peripheral parts, usually affects the toes, feet and legs, and more infrequently is distributed over the corresponding portions of the upper extremities. It may be considered as of two distinct varieties, each having an essentially different cause. Irrespective of the source of immediate inducement, such as external or even internal exciting factors, the blanching in thrombo-angiitis obliterans seems to have two absolutely diverse modes of creation, so that we may speak of:

- I. Mechanical or hydrostatic ischemia.
- II. Vasomotor ischemia.

I. MECHANICAL OR HYDROSTATIC ISCHEMIA

Pallor or ischemia is evoked by elevating the limb from the pendent position *to that extent which is incompatible with arterial influx into the vessels and capillaries of the skin*. With healthy arteries and adequate heart action the normal arterial *vis a tergo* is adequate to deliver blood into the most peripheral parts of the foot, that is, into the tips of the digits, and lend and conserve a pinkish normal blood tint in the distal skin areas. If in dorsal decubitus, the leg is raised to the vertical, any occlusive or obturating process in the chief arteries, makes such visible and customary color conservation impossible. Superadded to an abnormal diminution of blood supply in such a position is a certain degree of depletion and evacuation in the vascular system and one that conforms to the laws of gravity. In this sense, therefore, we may speak of *mechanical* or *hydrostatic* ischemia in obstructive, occlusive, obturating or obliterating types of vascular disease of the extremities.

Whilst vasomotor phenomena responsible for fugitive and transitory patches or even extensive areas of local syncope may be associated and confuse the clinicians' concept of *hydrostatic* ischemia, a careful comparative estimate of the phenomena, as they appear under various conditions, in any case, will usually permit of definite differential recognition. A knowledge of the coincidental occurrence of the two blanching phenomena is a prerequisite for a comprehension, not only of thrombo-angiitis, but also of the vasomotor and trophic neurosis so frequently confounded with it. A few tests, and subjective or objective considerations should suffice to distinguish the two types of ischemia.

Mechanical or hydrostatic pallor should be studied in the following way:
Relative to

1. The situation of its appearance.
2. The angle of elevation that brings it forth.
3. The time that must elapse for its definite establishment.
4. Its extent.
5. The arc in which pallor persists. Its complement will be the residual angle to which lowering of the limb must continue, for the restitution of a normal or reactionary red color (Angle of Circulatory Sufficiency, Chap. XXIX).

6. The persistence of well localized areas of ischemia even after return and reaction have been established by descent of the limb; especially when the phenomenon can be reproduced in the same situation by subsequent preliminary tests of elevation and depression.

From this summary it will be seen that the striking and distinctive feature of this form of ischemia, is its *dependence on, and variation with position of the limb*. By this it can at once be distinguished from the neurotic or vasomotor type.

1. Situation of Its Appearance.—As the leg is elevated, pallor is seen to replace the usual rubor that pendency brings on. The toes and then the foot become abnormally pale, the veins flattened and depleted, the peripheral digits often evidencing patches of cyanosis that may persist throughout the period of elevation. The simultaneous blanching of the toes and foot, possibly coupled with arteriovenous depletion throughout the leg, suggests arterial occlusion of greater degree or greater inadequacy of the collateral circulatory paths. Occasionally by irregular sequence, the pallor of the foot may antecede that of the toes; one of these, usually the big toe, may remain cyanotic and even the other toes may evidence a mottling or redness due to intracutaneous hemorrhages; or, other variations may be noted.

Certain adventitious factors contribute to the difficulties attending the correct estimate of the appearance of pallor. Thus, a continued cyanosis, particularly in cold weather, or transitory vasomotor irritants exciting even blanching in the pendent position, must not be confused with hydrostatic conditions. For it is the latter alone that are of value in diagnosis of the malady and in the appraisal of the degree of vascular obliteration. We must await, therefore, altered circumstances, give aid by establishing a proper environmental temperature state, and allow for psychic repose before making a test for the appearance of ischemia.

Pallor on elevation may affect only a few of the toes at the outset (one, two or more); or, there may be successive blanching of one after another without orderly sequence, the intensive cyanosis and rubor being recalcitrant and abolished with difficulty through action of gravity.

An extraordinary degree of blanching of a single toe, associated with chronic cyanosis in the pendent position, warrants the suspicion that gangrene or trophic disorder is imminent.

When the feet are very cold and apt to be cyanotic, as often occurs in winter, a combination of rubor and cyanosis permits only very slow and patchy replacement of color by yellowish white areas over the toes, until a considerable time has elapsed.

2. The Angle of Elevation That Produces It.—Theoretically this should be but slightly greater than that at which reactionary rubor is called forth. In truth, however, the two do not correspond, since, for a given time a distinctly greater elevation is required to establish pallor, than the minimum angle at which it still persists. Thus, if we have to elevate a limb to 170° to evoke ischemia, we may find that pallor still exists when the leg is depressed through a considerably larger arc than 10° . In a severe case with marked circulatory impairment, it is not unusual to find ischemia established at 135° or less, and continue for an indefinite time in the horizontal (90°). In other instances pallor ensues almost at once on elevation to the bed level (90° or horizontal).

When the degree of inducible blanching is doubtful or slight, a good comparative estimate of the two limbs may be attained by resorting to one of the following two methods; to,

(a) The repeated elevation and descension of the limb, two, three times or oftener, with possibly, coincident production thereby of a reactionary rubor during pendency, may evoke an ischemia otherwise concealed; or

(b) Careful observation of plantar aspect of the foot as it is raised and held up, in varying positions with the patient prone and the leg flexed through varying angles. Frequently distinct pallor is noticeable with the leg vertical (90°).

3. Time Interval for Its Establishment.—Employing approximately the vertical (180° elevation) as a routine test, this generalization is acceptable, that the more rapid the onset and completion of ischemia, the greater the extent of vascular obturation. We must view both dorsal and plantar surfaces of the foot, and even the leg with careful scrutiny and with adequate but not too glaring illumination, for a dependable appraisal of this valuable sign.

Where chronic cyanosis has set in, it may completely nullify the quantitative value of this proof of circulatory disturbance. Under such circumstances we are, however, usually dealing with severe and extensive forms of vascular obliteration.

Hemorrhagic infiltration of the skin and subcutaneous tissues, as also pigmented areas, the products of previous disturbances, may give confusing mixtures of colors that vitiate the general pallor that is to be expected.

A comparison of color phenomena displayed in the two legs will give valuable information as to prognosis, since the more extensive involvement is usually distinguished by more rapid evolution and greater distribution of the ischemia.

4. Extent of Ischemia.—Usually, by virtue of the advanced condition of vascular obliteration existing even at the first consultation, pallor on elevation is apt to involve the whole of the foot and more or less of the distal third, half or even two thirds, of the leg. Occasionally one toe alone, or several of the toes will show definite blanching whilst an appreciable color change is difficult to elicit elsewhere. It may, however, be persistently confined to the same number of toes, this localization lasting for a variable time yielding to more extensive blanching as the inadequacy of collateral, and implication of additional arteries advances.

Where ischemia is well established in the horizontal position it is usually limited in extent, rarely occupying a greater territory than the whole foot, often restricted to one half of the foot or to some of the toes.

Careful continued and repeated observation over weeks and months may reveal the striking fact, that ischemia may disappear, sometimes together with the rubor and the trophic disturbances. These are the cases of arrested symptoms and so-called "cures." In some of the quiescent cases all other signs (except lack of pulsations) may disappear, but ischemia on elevation will endure for years.

Per contra it is more usual to witness the reverse, namely, gradual increasing intensity of blanching associated with progressiveness in the other phenomena.

It is not uncommon to find seemingly inexplicable vagaries in the location and intensity of the white patches, and also coincident lividity. The significance may be better appreciated from a rehearsal of an instance such as the following.

In case, M. S., after elevation of the leg, the pallor is admixed with patches of cyanosis that almost look hemorrhagic. These are distributed over the big toes, being most prominent over their plantar aspects. Complete ischemia is very hard to elicit because of the

persisting cyanotic areas although some look hemorrhagic. They can be proven to be foci of stasis because blood can be dislodged by pressure converting them into pallid spots. Not dissimilar lividity accompanies localities of imminent gangrene; but such do not become pale.

Even after the induction of reactionary rubor which may begin over the ankle and spread slowly over the dorsum and plantar aspects of the foot, a larger or smaller area of pallor may remain either over the dorsum or the toes. Suddenly rubor may loom up in a distal part, leaving here and there a mottling of white. The tip of the big toe may remain white the longest, retaining a slight livid hue. Such a phenomenon is evidence of the poor circulation in the big toe, especially when it is last to regain a pinkish tint. When it becomes necessary to bring the leg to the pendent position to effect the latter, a valuable hint as to the gravity of the prognosis in this locality is at hand.

5. Arc or Angle of Persistent Ischemia.—Since this is the complement of the *angle of circulatory sufficiency* the phenomenon of blanching and its behavior on depressing the leg after prior ascent, will merely be touched upon here. Generally speaking, the greater the arc within which ischemia continues to remain in evidence the more extensive the arterial occlusion. A limb that remains blanched in situations between 180° (vertical) and 70° (20° below the horizontal) is one whose circulation is badly compromised. More frequently reactionary rubor is perceptible before descent reaches the horizontal. Although this angle cannot be estimated with mathematical accuracy, an approximate appraisal will suffice as a good working guide. This absence of precise delimitation between disappearance of ischemia and reentrance of rubor, is responsible for the inaccuracy of the test. Thus pallor over certain toes or even part of the foot may be difficult to dislodge and on the other hand, rubor may develop in patches that alternate with recalcitrant areas of pallor. If sufficient time be allowed to elapse, however, the reactionary rubor will finally disappear and cause every vestige of ischemia to vanish.

6. The Obstinate Areas of Pallor.—When one or more toes or areas, on repeated examination fail to become red when the test for reactionary rubor is made, and when such well localized spots of sanguinous depletion are visible even at the horizontal or at an angle of greater depression, we then have valuable evidence of marked local deficiency of circulation. Such areas are apt to be the seat of gangrene, at no remote date. When there is a history of spontaneous blanching in the same locality, or such discoloration after a walk in the cold, or when the situation of the pain coincides with the distribution of the pallor, strong corroborative testimony of impending gangrene or trophic disorder is in our possession.

II. VASOMOTOR ISCHEMIA IN THROMBO-ANGIITIS OBLITERANS

Since local syncope is discussed elsewhere, and many of its striking features defined in detail, it will be merely necessary here to allude to that perplexing association of pallor of neurotic origin, with the multiform color manifestations of mechanical or hydrostatic causation. For, even in organic maladies of the vessels where objective signs are eminently due to vascular obliteration, a *coincident display of vasomotor phenomena* may create a confusing clinical picture. A narration of the clinical manifestations alone will be attempted, since the explanations of such occurrences are still too vague and unsatisfactory to warrant argumentation. Suffice it to say here, that the implication of the nerves, and the perivascular chronic inflammatory process so noteworthy in thrombo-angiitis obliterans, may be responsible in part at least, for a loss of normal vasomotor stability.

To what extent metabolites, or a vicarious functional implication of the autonomic action of the capillaries and arterioles is responsible for these phenomena, future investigation may help to clarify.¹ Furthermore, it has been the contention of a number of physiologists, that a vasomotor constriction may be the sequence of ischemia alone whenever a part is artificially depleted of blood, just as a hyperemia is incident upon subsequent filling of the emptied vascular channels. In conformity with this hypothesis, a neurogenic reflex can play a rôle whenever there is abnormal anemia or plethora.

Too much emphasis cannot be laid on the fact, however, that most of the objective symptoms regarded and described by many authors as of neurotic foundation, are merely hydrostatic and compensatory phenomena; although, it is true, independent vasomotor disturbances may be concomitant and clinically mystifying in appearance.

Vasomotor ischemia in thrombo-angiitis obliterans seems to be especially influenced by *cold* and *exertion*; it is independent of posture, since it may occur in the horizontal and pendent positions as well as in the elevated. It differs, too, from hydrostatic and mechanical ischemia in that it may come on without apparent cause, alternate with rubor, and offer thus a variegated display of color tints that stamps the phenomenon as the result of a neurotic agency.

Especially notable are such manifestations when they occur in cases of thrombo-angiitis obliterans in which other objective pathognomonic signs have not developed sufficiently to warrant a positive diagnosis.

Since these manifestations are frequently more pronounced in the early stages of thrombo-angiitis obliterans than later in the course of the malady, diagnostic uncertainty must necessarily exist in the minds of those not thoroughly conversant with the relative significance of the two types of ischemia. An interesting example of the independent occurrence of the two varieties of pallor may be worthy of consideration.

Vasomotor Phenomena in Only One Leg. *Usual Clinical Course of Organic Vascular Disease in Both.*—H. R. presented simultaneously striking *vasomotor* signs in the *right*, and typical objective symptoms of thrombo-angiitis obliterans in the *left*. Later, whilst under observation, the vasomotor phenomena gradually disappeared, the disease taking its usual course in both extremities.

Thrombo-angiitis Obliterans Symptoms in the Left Leg, December, 1, 1908.—On taking off the shoe the left foot appears markedly red; the dorsalis pedis, posterior tibial and popliteal arteries are pulseless; there is marked ischemia on elevation.

Vasomotor Signs in the Right.—At the same time the right foot was found blanched in the pendent posture, cold, and patches of cyanosis appeared. *All the vessels pulsate.*

On December 24, the picture was still more striking. At this moment the progressiveness of the malady was noted by the *disappearance of both posterior tibial and dorsalis pedis pulses* on the right.

Upon taking off the shoes and stockings and examining the lower extremities, the difference in color between the left and right foot is remarkable. On the left the swollen and enlarged toes are of a deep red color, the hue extending up the dorsum of the foot is most intense on the inner side of the foot and fades off gradually towards the ankle. The right foot is of a peculiar yellowish white color, the toes are most markedly blanched and are distinctly smaller than on the left foot. (*Angiospastic pallor of the right foot in pendent position.*)

After the feet hang down for about five minutes their color changes. The color of the left becomes admixed with a blue tint, which gives a livid appearance to the foot, the purple color being particularly striking over the toes; here and there bright scarlet patches stand out prominently between areas of cyanosis. The right foot still retaining its more slender appearance has become cyanotic, the distal phalanges being of a deep dusky purple unmixed with any tinge of red, and the rest of the foot also shows a cyanotic hue but somewhat toned by a pale ashy skin, which shines through in many places. After the right foot has

¹ See Chap. VII concerning the independent action of capillaries and arterioles.

remained in the horizontal position for about five minutes, a little of the normal color appears over the fourth and fifth toes, but the first three toes are still quite blue.

After cyanosis had set in, however, *ischemia dependent on elevation could regularly be demonstrated in the right foot—this being the noteworthy diagnostic point in favor of thrombo-angiitis obliterans.*

March 1, 1909, amputation of the left leg. In November, 1908, the angiospastic condition in the right foot had disappeared, the popliteal artery no longer pulsated, the disease evidently making progress.

January, 1919, amputation of the right leg; specimen showing typical lesions of thrombo-angiitis obliterans.

Conclusions.—A period of vasomotor disturbances as predominating objective sign in the right leg; rapid development of thrombo-angiitis obliterans in the left with amputation; disappearance of vasomotor phenomena in right, followed by usual symptoms of thrombo-angiitis obliterans.

A further discussion of this type of blanching is relegated to the chapter on *Vasomotor Symptoms in Thrombo-angiitis Obliterans.*

Ischemia, an Index of Circulation.—We have elsewhere alluded to the value of the angle of circulatory sufficiency as an approximate *clinical* measure of the circulatory condition; and also to the fact that the obstructive effects vary in inverse proportion to the size of the angle (above the horizontal) through which the limb must be elevated before pallor is established. In acute exacerbation of any of the organic types of vascular occlusion, when either by virtue of extension of the disease *per se*, or through superadded accretion, bland or mechanical thrombosis, new vascular territories become involved; these methods of circulatory appraisal become even more reliable and valuable—for compensatory collateral paths (an otherwise misleading factor) have not as yet become adequately established.

If cases of atherosclerotic disease of the arteries can be observed during and after attacks of thrombosis, we can note subsequent improvement of the circulation, not only by the usual signs, but also by estimating the altitude to which elevation of the leg is necessary for the advent of the first signs of blanching. Very frequently, ischemia is present even in the horizontal position, shortly after thrombosis or embolism. As the limb improves, the leg must be raised higher and higher to elicit the ischemia. Early in the clinical course of the embolic and thrombotic cases, a production of the blanching is easy, for then a very slight raising of the limb above the horizontal is apt to produce it.

These observations apply also to other forms of organic vascular maladies where obstructive conditions of the circulatory channels are at hand.

CHAPTER XLVI

THROMBO-ANGIITIS OBLITERANS—ERYTHROMELIA¹

Erythromelia,² *Rubor*, *Hyperemia*.—We may divide the rubor accompanying this affection into (1) inflammatory, (2) non-inflammatory or intrinsic rubor, and (3) the vasomotor.

Types of Rubor.—1. *The inflammatory rubor* or hyperemia hardly requires comment, in that it is associated with inflammatory processes, differing only in so far from the reactive redness of the normal, that it is apt to be less

¹ For other interpretations of erythromelia in the light of the findings of capillary microscopy, the reader is referred to Chap. CVII.

² This term must not be confounded with that of "erythromelie" proposed by Pick for the disease, Idiopathic Atrophy of the Skin (see Chap. Scleroderma).

intense in the neighborhood of trophic lesions than we would expect with healthy vessels. Edema and lymphangitis are often coexistent lesions.

2. *The intrinsic rubor or "erythromelia"* (as the author has termed it) seems to be due to compensatory dilatation of the superficial capillaries. This manifestation has led to much confusion in the differential diagnosis between *erythromelalgia* and thrombo-angiitis obliterans. It is a red blush of varying degree or intensity, that usually begins in one of the toes (big toe especially) and extends over all the toes for a variable distance up the dorsum of the foot. It may be so slight as to necessitate comparative exposure of both feet for its detection, or so marked as to partake of a crimson or vermilion hue. Its appearance is enhanced in intensity and expedited in developing by allowing the limb to hang down, the color increasing gradually until it attains its maximum, when a slightly cyanotic tint is wont to be admixed, whilst the dorsal veins of the foot attain their maximum prominence.

When rubor is present in any position between the horizontal and the pendent, when it is manifest at room temperature in these postures, we term it *chronic rubor or erythromelia* in contradistinction to that rubor which is *induced* after preliminary elevation of the limb. The advisability of making so subtle a distinction will be made clear when the importance of the two manifestations in diagnosis will be discussed.

Chronic rubor or erythromelia is an inherent, characteristic and unmistakable stigma of defective circulation in the deeper vessels and its chronicity and dependence upon posture of the limb should at once differentiate it from the rubor of *vasomotor* origin. It is not only influenced in intensity as the limb is elevated or depressed, but suffers change secondarily through any circulatory alteration that may be transmitted to the deeper vascular channels. As elevation of the limb empties the deeper channels, so also, will blood be drawn from the superficial parts, both through evacuation by gravity, as well as by diminution of the supply. Variations in erythromelia upon changes of position are greatest where the deep vessels are most extensively diseased.

Mere elevation to the horizontal may decrease the redness considerably, while lifting the limb towards the vertical causes its complete disappearance.

The position (angle or level) at which the hyperemic manifestations appear is subject to variation. Sometimes rubor is apparent with the leg elevated slightly above the horizontal, at the horizontal, or below this level. It is evident that these types must correspond to different degrees of circulatory impairment, the vascular obliteration being doubtless most extensive in the last type, or, per contra, the collaterals are least adequate.

Although erythromelia is a very constant symptom and usually appears at some time during the course of the disease, it may be continuously present in some, be absent in others, and in still other cases may persist for a long time, disappearing completely when the symptoms have abated or the limb is in a "cured state." In two cases (S. and J. R.) erythromelia remained for a considerable length of time, and then completely disappeared when the limb was free from symptoms.

Reactionary or Induced Erythromelia.—With the limb held high for a time, subsequent pendency is regularly followed by a reactionary or induced rubor of much greater intensity. This phenomenon is closely analogous to the hyperemic reaction that follows the application and removal of a constricting bandage to an extremity. Since ischemia must precede its production, its demonstrability indicates that a state of arterial occlusion or impaired circulation must exist. For, without occluded vessels, the mere elevation of the limb

is ineffective in causing the requisite blanching. *The importance of reactionary or induced rubor* in the recognition of obturated deep vessels can thus readily be realized. In a routine examination of cases of suspected arterial occlusion, the contingency of appreciably altering the degree of rubor by a preliminary lifting of the limb must be considered. And it is always advisable, therefore, in order to gain a correct estimate of this symptom, to examine the extremity first, in the dependent position (as the patient walks into the office), second, in the horizontal position, third, in the elevated, and finally, again in the pendent, when the *reactionary* or induced rubor will be viewed.

Partly by reason of thermal constricting influences (vasomotor), and partly for other reasons, it is not always feasible to demonstrate a very noticeable reaction. In such cases, the procedure of elevating and depressing the limb must be repeated two or more times, in such a manner as to permit ischemia of one minute duration to be followed by a reactionary period of about three minutes or more. We will not infrequently be rewarded by thus evoking a most exquisite rubor that seemingly could not be elicited at all.

Not only is this a valuable diagnostic sign in indicating the existence of arterial occlusion, but may be utilized to differentiate between the relative activity and extent of the obliterative process in the two limbs. Furthermore, it may be exhibited at a time when the chronic rubor is so slight as to be doubtful. Fine distinctions, such as a color reaction in the horizontal position in one limb, and in the position of complete pendency in the other, with appearance over the leg before it reaches the toes and foot, are amongst the variations encountered.

Reactionary erythromelia is frequently of value in the diagnosis of those cases, in which, for a long time, there are no symptoms other than pulseless vessels (possibly only the dorsalis pedis), and pain. In these, fairly marked induced rubor may be present long before the characteristic chronic rubor develops.

Thus, in one case H. F., absent dorsalis pedis and posterior tibial pulses, with reactionary erythromelia were the only signs of thrombo-angiitis obliterans. Ischemia was doubtful. Later on (June 11, 1910), a slight chronic erythromelia appeared. Under our own eyes erythromelia developed, but for a long time we had to have recourse to the reactionary rubor in making the diagnosis.

A careful scrutiny of the color changes accompanying the induced rubor may lead to conclusions of diagnostic and prognostic importance.

With the advent of the reactionary erythromelia in certain cases, it is very interesting to note how certain portions of the foot will remain white longer than others. By digital compression of the hyperemic areas, the rapidity of hyperemic return will show differences of circulatory activity in various toes.

To cite an example:—In the case S. L., all of the toes and an inch and a half of the dorsum remained white for 3 or 4 minutes, although the rest of the dorsum became very red. The return of blood into the toes was not simultaneous, but the fourth and fifth showed rubor, whereas the first, second and third remained white. Patches of white also persisted over the dorsum. The big toe of the right foot remained white for a long time, and the reactionary erythromelia existed much longer in the foot that was markedly affected than in the other in which the symptoms were slight.

Other variable phenomena associated with induced rubor are of no mean value in the acquisition of a general concept of the pathologic conditions at hand. Evidences of inadequate circulation are notably enhanced by the

induction of this type of rubor. The observations in the following case will illustrate.

In the case, M. S., the *reactionary erythromelia* begins to appear over the left ankle extending slowly over the dorsum and plantar aspects, leaving a large and small area of *pallor* over the dorsum and the toes for some time. Then it looms up at a more distal part, leaving here and there a mottling of white. Remarkable, however, is the fact that the *tip of the big toe remains white* longest, and with it there is an admixture of cyanosis. A similar condition obtains in the right leg but not so marked. It is necessary to depress the foot to obtain rubor of the big toe.

In short, here are phenomena expressive of the *poor circulation in the big toe*, since it is the last to regain its circulation; and here is exemplification of the value of inducing rubor to confirm signs that might be misinterpreted as of vasomotor origin. For, indeed, localized syncope may occur even in organic obstructive arterial affections.

Cold and vasoconstriction from other causes may temporarily prevent the demonstration of both chronic and induced rubor. So it may be necessary either to warm the extremities affected or to artificially further the dilatation of the superficial vessels by repeated changes of posture. The latter is done by elevating the limb for 1 minute, so as to produce ischemia, then to depress it for 2 minutes. Several changes of position will eventually evoke a reactionary rubor that may be otherwise indefinitely postponed by reason of vasoconstricting influences.

Duration of the Chronic Rubor.—When the postural treatment of the author is successful in dispelling most of the symptoms, then we often note a disappearance of the chronic erythromelia. Such disappearance of the chronic rubor with a slight reactionary rubor, however, can be elicited even when erythromelia is absent.

In short, the chronic rubor disappears before the reactionary. The following case will exemplify.

J. K., 37 years of age, November 24, 1920, presented the typical history and physical appearance of thrombo-angiitis obliterans involving both lower extremities, and the development of an ulcer of the small toe, and another between the second and third toes of the left foot. These have not healed.

A deep ulcerating fissure at the base of the little toe is observed, the foot in a state of chronic rubor, the big toe slightly tumefied, and an ulcer over the small toe. The dorsalis pedis and posterior tibial pulses are not perceptible. The postural treatment was prescribed.

April 14, 1921, still marked rubor of the left leg and absent pulses of the right are recorded.

October 24, 1921.—The chronic rubor has disappeared completely, but the dorsalis pedis and posterior tibial arteries are still pulseless; postural treatment continued.

October 16, 1922.—Both feet have a *normal* appearance; disappearance of the chronic rubor, but *reactionary rubor* can still be elicited, but of slight degree. His symptoms have almost disappeared, demonstrating (1) the value of the postural treatment; (2) the disappearance of the chronic rubor; and (3) the persistence of the reactionary erythromelia.

A similar change in the character of the rubor is not uncommonly noted in the upper extremities, where, however, the restitution to a normal appearance of the hand is more striking than in the case of the lower extremities. The reactionary rubor persists long after the chronic rubor has disappeared.¹

3. *Vasomotor rubor* may enhance an existing intrinsic or chronic rubor, but more frequently is a patchy hyperemia of small extent interspersed with areas of pallor. It may be reactive and follow that abnormal pallor of the foot which is induced by cold. More data on vasomotor phenomena will be given in Chap. LIV.

Significance of Rubor.—Whilst we do not expect a formal and definite reciprocation between the dilatation of the superficial vessels and the quantita-

¹ See p. 298, case R. L.

tive organic inroads on the deep circulatory channels, a partly abortive and partly successful attempt is nevertheless made here by Nature to improve the delivery of blood. This is accomplished, probably, by inhibition of vasoconstrictor stimuli (or stimulation of vasodilators); but just how, it is difficult to determine. In contrast with the establishment of the functionally more potent deep collaterals (Chap. XII), this generalized tegumental and subcutaneous vascular ectasia is but a vicarious attempt. Reasoning *a posteriori* from the beneficial effects of the author's postural treatment,¹ it must be regarded as an index or partial measure of an accompanying enhancement of vascular girth and patency in the deeper arteries.

In the "postural" procedure we call forth hyperemia by an artificial sequence of changing positions. Knowing that induced rubor will follow the preliminary blanching produced by elevation, we posit, therefore, that such reactionary rubor—which is but a heightened erythromelia, and only the external visible characteristics of which are perceived—is valuable, not only through its amelioration of the skin circulation, but also because it may be, and probably is, associated with similar angiectatic or expansive phenomena in the muscular and other deep arterial branches.

A number of interesting phenomena attest the heightened vasomotor instability of the vessels supplying the skin, when either chronic, induced or both types of rubor become visible. Thus, the occurrence of irregularly outlined and evanescent areas of pallor, interspersed amongst the general redness that is evoked by elevating and then depressing the limb, is a manifestation of more severe impairment of circulation in the limited ischemic area, or merely significant of a prolonged angiospasm. Setting aside the former type which is evidence of chronically impoverished circulation for consideration elsewhere,² let us appraise the importance of the observations from which the vasomotor nature of the latter has been deduced.

We have already noted that when induced rubor is elicited, certain fugitive spots or areas of pallor will outlast the general ischemic color, but will, after a variable time, also be replaced by redness. What causes these pallid spots? Why is the blanching so transitory?

Upon reflection it will be admitted that but three explanations are applicable. Either there is a permanent narrowing of the arterioles and capillaries of these parts that is more intensive than in the surrounding area; or, the *vis a tergo* is insufficient to fill these as quickly as elsewhere; or a vasoconstriction is present, which outlasts any such phenomena that may have been present in the adjoining parts. Of these three different views, the last seems to be the most plausible explanation.

Noteworthy and significant is the fact that the transitory type of persisting ischemia does not affect exactly the same areas on all occasions, but even during the same interview and examination, repeated tests for induced erythromelia may bring forth varied pictures. Certainly, therefore, an organic cause cannot be ascribed to the phenomenon.

Furthermore, it is not the most distant parts that are the seat of it, the dorsum of the foot at points considerably removed from the tips of the toes evincing it as frequently as the most peripheral parts. Therefore, an incompetent propelling force from behind is also not responsible. *The bizarre colored appearance should, therefore, be attributed to an unstable nervous mechanism.*

¹ Postural treatment is described on p. 380.

² See Chap. XLV.

We believe that immediately on elevation of the leg and particularly through prolongation of this position an arterial constriction may occur, as a necessary functional and compensatory action. For, the diminished arterial supply through the scant vascular channels and the reduced *vis a tergo* in the distal parts, accounts for collapse of vessels when blood has to flow up hill. A vasomotor constricting influence is the necessary sequence, though its occurrence cannot be predicated for all cases. Depressing the limb, since it causes a sudden inflow, should normally evoke a relaxation of the contracted vessels. In fact this occurs in the areas that are the seat of reactionary rubor. Pallid zones then, are those in which such vasodilatation is temporarily in abeyance.

Where more or less permanent, identically situated ischemia, oft attended with cyanosis, is a feature in the peripheral part of a digit, or other distal part of the foot, organic vascular occlusion is usually the cause.

Explanation of Erythromelia.—An attempt was made by the author to investigate clinically whether the dilatation of the capillaries and arterioles producing chronic rubor was of paralytic nature. The induction of dermatographia suggests that in most cases, a true palsy of the capillary activity does not exist. The observation that cases lose their chronic rubor when they improve after the postural treatment, also speaks in favor of this conclusion.

If we cause the red type of dermatographia (dermatographia rubra) in a foot that is in a state of chronic rubor, and subsequently bring about ischemia thereof by elevation, blanching of all of the skin is produced, the reacting streaks showing slightly as very faint bluish red lines, or not at all. On subsequent depression of the foot, it will be seen that the reactionary rubor may appear *first* in the streaks of dermatographia and *later* in the immediately surrounding areas. This would seem to warrant the conclusion that there has been produced a distinct comparative alteration in the tone of the capillaries of the scratched areas, one that temporarily puts these into a state of dilatation, whilst the surrounding parts yield to the reflexes gradually and show belated dilatation in the pendent position of the limb. If complete palsy of the capillaries were present, no such difference in time of response should exist.

Whether the delayed rubor indicates belated reflex dilatation or slow chemical response on the part of the capillaries, is an open question. At any rate, *the conclusion is warranted that the finer vessels are still able to respond, and are not wholly inert and paralytic.*

Can we satisfactorily account for the striking rubor so characteristic of this affection, and of other obliterative arterial diseases? To state that it is a compensatory phenomenon is merely an expression of a teleological view, and an assignation of a distinctive attribute to the phenomenon. We can obtain illuminating information on its *modus operandi*, however, by intensive clinical and anatomical studies. From such, the author would offer the following explanation.

We assume that with the exclusion of the normal major circulatory channels, although there is a generally diminished pressure, a relatively larger amount of blood tends to remain in the superficial arterioles and capillaries. This blood arrives through devious channels by circuitous routes, and by virtue of the diminished *vis a tergo* must needs remain longer in both arterioles and venules. In short, a sluggish circulation with stasis is the result—an inference that receives confirmation in the fact that the

“expression test” (compression of the skin) always indicates a tardy return of blood into the integument.

Does not this stasis in the arterioles and capillaries exert an effect which impresses itself upon, and evokes a response in the vasomotor innervation? We must answer in the affirmative. For, although anatomical alterations in the nerves accompanying the arteries (perineuritis) are concomitant lesions of thrombo-angiitis obliterans, these alone cannot be responsible; this, because rubor occasionally comes on rapidly after a sudden accession of thrombosis in arteriosclerotic cases, where no perineural changes have been found. *Erythromelia may be of rapid advent, signalize, and be synchronous with other evidences of an attack of acute thrombosis. In such, a neuro-anatomical and pathological causal basis can be excluded, and we must expect alterations in functional innervation as the creative grounds for the phenomenon.*

With the limb pendent, the constant stasis in the arterioles and venules then—whose existence is adequately corroborated by the color changes elsewhere described—may be regarded as influential in producing a state of chronic vasodilatation with partial exhaustion of the vasoconstricting mechanism. That complete paralysis of the constrictor power does not occur, is proven by the occasional local syncope that goes with, and alternates with rubor in certain cases, and by the circumscribed and limited areas of pallor that outlast the generalized rubor, when the test for ischemia and induced erythromelia is carried out, and by the response to dermatographia occasionally elicited.

In short, we postulate a maladjustment, malfunction and instability of the vasomotor mechanism, as the result of continued disturbance in the normal intravascular pressure. What is more likely than relaxation of the normal arterial tonus when the small vessels have lost the aid of the usual *vis à tergo* in the propulsion of blood through the tissue and back through the veins? Their muscular mechanism, just as in other viscera, may suffer; and they may lapse into a state of chronic dilatation, which we have elsewhere regarded as compensatory. In most instances however, their contractility is at least partially conserved.

In erythromelia we presuppose an inhibition of the vasoconstrictor impulses, incited, accompanied and aided by hydrostatic conditions. In the usual ischemia on elevation or even in the horizontal position, we are dealing merely with a hydrostatic phenomena, one of pure depletion; although (as has been elsewhere pointed out) subsequent vasomotor contractions may supervene, and prevent for a time at least a rapid refilling of the vessels when the proper conditions of gravity (pendent position) are again restored (neurogenic ischemic reflex).

In consonance with this conception, we predicate a division of the vasomotor phenomena into two types:—First, that of central origin (as in Raynaud’s disease, erythromelalgia and the other vasomotor and trophic neuroses), and secondly, an essentially peripheral form (thrombo-angiitis obliterans, arteriosclerosis, and the other obstructive arterial diseases). Whilst the deranging nerve impulses in the neurotic type emanate primarily from the central nervous system, the aberrant vasomotor responses in the organic vascular processes, owe their origin to abnormal impulses from the periphery. Although this view is acceptable as applying generally, it must be qualified in so far as it does not imply that centripetal stimuli play no rôle in inciting the unstable nerve mechanism of the vasomotor neurotic type, nor that emotional, and other central agencies may be altogether impotent in

the organic arterial maladies. A more complete exposition of this subject is to be found in Chap. LIV.

When we speak of *compensatory dilatation*, we unwittingly seem to inject a teleological interpretation into effects whose origin may be wholly passive. But for the student, such inferential thinking serves a good purpose in emphasizing certain objective and therapeutically adaptable phases of the phenomena; and, therefore, is wilfully allowed to be incorporated here.

If we were to attempt an explanation based on mechanical or hydrostatic laws alone, we would err in not having taken into account the nerve mechanism, the autonomic action of the capillaries themselves,¹ and the possible secondary paralytic and exhaustive influences occasioned by the unusual obstructive impairment of circulation. Taking these forces into consideration, it would seem that all do not participate to an equal degree, or else the varied pictures, with or without fleeting vasomotor phenomena could not be explained.

A detailed discussion of the rôles of the numerous motivating and determining elements is given in Chap. VII on Physiology of the Capillaries. Here, we need but summarize our theories that superficial arterioles and capillaries may attain a more or less chronic state of dilatation as the result of the following causes.

(1) Exhaustion of the vasoconstrictor mechanism of primarily mechanical origin.

(2) Local action of metabolites or katabolic agents in a field of impoverished nutrition.

(3) Action of specific toxins on the autonomic capillary regulatory functions with paralysis of these.

1. The Exhaustion of the Vasoconstrictor Mechanism.—With more or less constant collapse of, or diminution in the size of the arterioles and capillaries, we would have to assume, according to the accepted views of physiologists, that a chronic increased tonus in these vessels must be the response. How long can this continue without yielding to that paralytic stage which would objectively find its expression in the clinical state of erythromelia? But that this cannot wholly account for the altered vascular girth is demonstrated by the clinical phenomenon that with existing rubor, vasomotor syncope, transitory, localized, fugitive, but nevertheless present, may occasionally be conspicuous. How then could we reconcile an exhaustive or paralytic state with one still capable of responding to a nerve mechanism?

Whilst seemingly diametrically opposed conditions, these are not so diverse as they would appear at first glance, for, firstly, the vasomotor syncope but rarely occurs when the hydrostatic factors are still at play, as in the pendent position, and secondly, such fugitive neuromuscular activity as angiospasm can be dispelled and actually exhausted by the clinical method of inducing rubor already described (reactionary or induced erythromelia).

As for the first contention, we note that vasomotor syncope in the pendent position is more apt to occur in those cases in which the disease has affected but limited and shorter territories, as in the clinically early or little advanced case; namely, in those in which exhaustion may be but partial and the vessels are still amenable to nerve influences. And secondly, by passive exercises in which the dynamics of hydrostatic and gravity nature are summoned into play, an actual insufficiency and exhaustive state of the capillaries and arterioles can

¹ Vide, also Chaps. XIII and LXXXVII.

be demonstrated. For, given that syncope of neurotic nature in thrombo-angiitis obliterans which but occasionally qualifies the picture, its fleeting nature can be readily recognized in the case in which the changing position of the limb may cause it to disappear.

Nor must we interpret the absence of rubor in the horizontal position as an argument in favor of retained vasoconstricting powers. For, in such position, the force of the circulatory stream may be inadequate to force the blood through the collaterals and into the capillaries. Unfortunately, the effects of gravity must sometimes be called to aid in the production of rubor, so that an additional mechanical factor is injected.

2. In consonance with the work of recent investigators, we must take into account that the **products of local metabolism** are believed to be a potent factor in producing dilatation of the smallest vessels. Are not metabolites present in increased abundance in territories so badly nourished? Just what part is played by the chemical influences is still a matter of conjecture. That a vicious circle may be produced in areas (toes) that are in imminent danger of gangrene, seems more than likely, for that stasis occurs is clinically often demonstrable.

Perhaps this excessive stasis that leads to cyanosis is furthered by the dilated condition of the capillaries.

Whilst it may seem paradoxical to recognize the possibility of chronic dilatation of capillaries and venules, and to question the likelihood of a continued state of tonicity without exhaustion, more careful reflection will explain this seeming inconsistency of thought. Whereas a state of dilatation, passivity or inactivity can be comprehended as of unlimited duration, an active constricted state, be it due to neuromuscular incitement (arterioles), or even to an inherent contractile power of the cells themselves (capillaries) may have its limitations in time, and yield to exhaustion.

3. **Specific Toxins.**—This last is purely theoretical and can hardly obtain except in pregangrenous stages, for rubor is produced by diseases of diverse pathogenesis. Whilst the hypothesis of the existence of such a poison in thrombo-angiitis obliterans could be entertained for the acute stages of the disease, the chronic obstructive stage with healed products in the vessels should offer chemical substances not essentially different from those elaborated as waste or by-products in the tissues in the other occlusive vascular maladies (arteriosclerosis, bland thrombosis, healed syphilis with thrombosis, etc.)¹

CHAPTER XLVII

THROMBO-ANGIITIS OBLITERANS—CYANOSIS

As a manifestation of impaired circulation, this phenomenon varies as to intensity, localization, and duration, and must be regarded as subject to vasomotor influences, as well as to obstructive circulatory factors. With this in mind, and with full cognizance of the influence of thermal and emotional factors, its rôle as a sign of thrombo-angiitis obliterans can be more accurately appreciated.

¹It may be of interest to note here that certain Russian observers believe that in the course of intravascular thrombosis, a ferment or toxin is liberated that in itself can bring about alterations in vasomotor function.

Although subsidiary in importance to the rubor, it is frequently present over one or more or all of the toes, and even over the whole foot, especially when the latter is allowed to hang down for a considerable time. Then a certain amount of purplish discoloration is wont to be admixed with the rubor that is so constantly present in this position.

In the elevated position of the limb, when blanching has already taken place, multiple cyanotic areas are apt to remain, often more marked in the toes whose circulation has been most impaired.

Cold has a decided influence in evoking and stabilizing an asphyctic state, the rubor giving way to it particularly over the very peripheral parts. But even under ordinary climatic conditions cyanosis of the toes is frequently intermingled with the rubor. Thus, the tips of the toes may be cyanotic whilst the dorsum shows marked hyperemia, and the plantar aspect of the foot may evidence patches of bluish purple discoloration.

When considerable circulatory obstruction is present, cyanosis in the dependent position may yield to ischemia in the horizontal or above the horizontal, but patches of more or less permanent cyanosis tend to remain.

In many cases cyanosis of the big toe is rather suggestive of the presence of the disease, and may be the only objective sign except for the absence of pulsations. That the diagnosis of thrombo-angiitis obliterans is warranted on these manifestations alone, the future course has demonstrated as well as the coincidental occurrence of the affection in the other leg where symptoms may be pronounced.

Local chronic cyanosis when it is limited to one toe may precede gangrene of that particular locality by months or even years. When it continues for a considerable length of time, we must be guided in making our prognostication as to the advent of gangrene by other signs, such as marked ischemia, a poor angle of circulatory sufficiency, and extensive obliteration of vessels. The persistence of localized and intense cyanosis, however, is always suggestive.

In such a case observed carefully for a year, the persistence of a more pronounced cyanotic discoloration of the big toe of the right foot was noted, the cyanotic color being much deeper in the big toe than elsewhere in the foot. This sign was more or less constant for some ten months, when the rubor was intense over the whole foot except for the deep asphyxia of the big toe. After eleven months of almost constant cyanosis *gangrene* appeared.

Such *chronic cyanosis* when edema, coldness, and localized anesthesia are superadded is no longer merely a sign of circulatory impairment, but augurs that gangrene is imminent. Amputation (Gritti-Stokes) undertaken in such cases has demonstrated extensive vascular occlusion involving even the popliteal artery although one or more vessels (such as the anterior tibial) may remain patent. It may be impossible even after careful anatomical investigation to establish a causal basis for the chronic cyanosis.

In a review of the histories of one hundred cases, the author found that seventy-one gave manifestations of asphyxia of one or more toes of either foot at some time during the clinical course, although it was not a significant sign at all. For, it is producible by a prolonged pendency even in the presence of rubor and may precede and accompany the incipency of gangrene. In eighteen cases *both extremities* simultaneously showed cyanosis, a percentage of bilateral involvement that might vary considerably and be much higher if a longer period of observation had been undertaken.

But cyanosis as well as ischemia (and the two often coincidentally) may be the expression of the concomitant action of mechanical as well as vaso-

motor causal factors. That this is true is evidenced by the observation, that occasionally the forepart of the foot may be markedly asphyctic, remain so for a considerable period of time ($\frac{1}{2}$ hour or more), and be irresponsive to such vasodilating excitants as changing posture (elevation and consequent depression) and heat. At other times, removed by but short intervals of time, both ischemia and asphyxia in the same foot are less marked, more evanescent and more readily abolished by the above mentioned means.

It is difficult to draw accurate conclusions as to the comparative importance of the *vis à tergo*, the hydrostatic and gravity elements, and the vasomotor influences in the determination of the intensity of local asphyxia. Enough observations are at hand attesting to the participation of all of these factors to varying extents. Perhaps most influential are the forces of gravity and inadequate *vis à tergo*, that allow of the accumulation in the veins and capillaries, and a certain degree of reflux of the poorly oxygenated blood. Thus, we could explain the intensification of the cyanosis of the feet in the pendent position, and the frequent disappearance of much of the asphyxia in the horizontal and elevated postures. Vasomotor lability and the possibility of venous spasm cannot be altogether excluded, however, as an occasional causative or coincident and participating agent. For, while lividity of the fingers may be noted in the hanging position of the arms where extensive arterial obliteration is present, considerable or even exaggerated asphyxia may persist on elevation, or even when the arms are in the horizontal position. The venules probably do not empty themselves, partly because arterial circulation is defective or almost in abeyance in these positions, and also because of complicating venous spasm.¹

An interesting case with marked cyanosis may be worthy of citation.

W. K. complains of pain in the feet at night and the inability to sleep. Walking is difficult because of the swelling of the left big toe and stinging pain. Two years ago he could not step on the sole of the right foot which was swollen. The left big toe is now especially painful and made worse either by raising the foot or lowering it.

Physical examination.—In the pendent position the tips of the toes of both feet are cyanotic, whilst the dorsal aspect of the toes shows rubor, more intense in the left than in the right. The left foot is larger than the right, its forepart being slightly swollen and the veins standing out more prominently. The sole of the right foot shows color changes, which are more marked over the forepart and involve four toes. The latter show numerous cyanotic patches, whilst the plantar aspect of the little toe is almost normal in color. When raised to the horizontal the right foot becomes ischemic. All the toes of the left foot and the distal half of the sole show marked cyanosis, but in a few minutes the purplish tint disappears, leaving the sole and the toes ischemic, except for patches of permanent cyanosis. The big toe is tender to the touch, although without signs of trophic disturbance. The dorsum, too, shows ischemia when the feet are in the horizontal position. Reactionary erythromelia of both feet can be elicited. The dorsalis pedis, posterior tibial, and popliteal arteries of both legs are absent.

Summary.—Intense cyanosis of the left foot, especially of the big toe; severe pain on elevation of the legs, now also in the pendent position. The right leg, previously attacked, is now in a latent stage.

Temperature conditions are not without influence in determining whether cyanosis will predominate over the chronic rubor. Thus, in the case cited below we quote from the notes taken on a cool and on a warm day, to demonstrate the preponderance of cyanosis in colder weather.

Case D. B. male, *on a cool day*—the right foot has a violaceous red appearance, the toes are livid, their tint composed of a mixture of deep bluish purple and bright red. Over the dorsum there is a mottling of red and blue. A similar condition obtains in the left foot with intensified cyanosis in certain areas, especially over the big and fourth toes.

¹ See p. 300, case S. S. S.

On a warm day—the toes of both feet are bright red up to their roots. This color deepens in the pendent position and is attended with increasing pain.

Pathogenesis of Cyanosis.—Cyanosis is perforce divisible into the types produced by the following causes:

1. Venous obstruction.
2. Diminution of arterial *vis à tergo*.
3. Vasomotor influences.

The most alluring explanation of the mode of production of cyanosis when the limb hangs down—and one accepted and taught by numerous clinicians—is that which presupposes obliterative disease of the veins as wholly responsible. Although such lesions may be a factor in certain cases, numerous pathological and clinical observations have demonstrated beyond peradventure that *cyanosis of intense degree is compatible with patent veins*. When vasomotor influences may be discounted or excluded, the true cause is to be found in the diminished pressure in the arterial system, which is powerless to propel the blood with the usual rapidity into and through the devious channels, stasis in the capillaries and veins being the consequence. The truth of this assumption is demonstrable by the simple experiment of reducing the requisite force for a prompt venous return. This may be done by mere elevation of the limb from its situation of pendency to the horizontal level, where the cyanosis will immediately diminish or vanish.

In some of the early cases¹ vasomotor instability is a decisive factor in the production of cyanosis giving an unusual clinical picture; this is often associated with syncope, the whole making a confusing complex that antedates the development of the pathognomonic composite of phenomena. Where vasomotor action accounts for cyanosis, it is assumed by many that a spasm of venules occurs, that is, vascular territories distal to the arterioles suffer spasmodic contraction. Thus, in Raynaud's disease even superficial veins, large enough to be examined by the naked eye, have been actually seen to contract in cases of local cyanosis, the asphyxia being thereby accentuated. Even contraction of the arterioles alone after producing local syncope may have as a natural sequence a superinduced cyanosis; and this by excluding the cardiovascular force—the *vis à tergo*—so that stagnation in the veins is to be expected.

When the technic will have become perfected and standardized, estimates of capillary pressure may give valuable information concerning the influence of diminished *vis à tergo* and the forces impeding the outflow of blood. Capillary stagnation produced by the former mechanism should be associated with low capillary pressure, and if by the latter, with high pressure. Dilatation of capillaries alone could, by reason of the diminished velocity of the blood, be followed by relative deoxygenation and cyanosis. This is the type that succeeds the rubor when the limb has been allowed to hang down for a time. In this position the *vis à tergo* is insufficient to adequately accelerate the flow upward through the venules and against the action of gravity. We would not expect that the cyanosis of thrombo-angiitis obliterans developing on rubor would be attended with an excessive capillary pressure, unless there is coexisting vasomotor spasm of the venules during an attack of temporary or fugitive vasomotor constriction. In such, spasm of the venules may occur.

Recent work suggests that through methods of estimating capillary pressure, much valuable knowledge may be gleaned as to the nature of

¹ Vide Chap. LIV.

asphyxia.¹ If increased pressure is found, spasm of the vessels may be assumed, and so the participation of a vasomotor factor is believed to occur. Perhaps the comparative rôles of the neurogenic and hydrostatic forces can thus be differentiated, for the latter can be wilfully altered by the position of the limb. So, the importance of such investigations, aside from a purely academic interest, lies mainly therein, that hydrostatic or mechanical factors, when of increasing importance, forecast an unfavorable outlook, and seemingly incongruous vasomotor manifestations are of relatively little significance.

CHAPTER XLVIII

THROMBO-ANGIITIS OBLITERANS—EDEMA

A peculiar puffiness of the toes together with an effacement of the usual irregularities of the dorsal aspect of the foot is often incorrectly ascribed to edema alone. Although from the pathological standpoint a slight edema pervades the tissues, there is also a chronic proliferative process in the subcutaneous tissues of the toes that contributes to the picture. This more or less permanent condition, which is so characteristic in the cases with intense chronic erythromelia, may continue for years. The toes and the forepart of the foot by reason of the disappearance of surface irregularities, acquire an artificial appearance as if molded in wax.

A transitory inflammatory edema if slight, accompanying, and due to the coexistence of trophic lesions such as ulcers and small patches of gangrene, is not at all an unusual feature nor one that need give concern. But another type of edema which is extensive and permanent is of great omen.

In a number of cases, most of which curiously enough belong to the severe type of the disease in which the prognosis as to the integrity of the limb is concerned, edema is a prominent feature. Days or weeks after the onset of the trophic disturbances, the dorsum of the foot first begins to show signs of extensive edema. This is unassociated with any phlegmonous process. In a number of these cases the author was able to follow the course of this phenomenon, and found that it often accompanied or preceded sudden aggravation of the condition in cases in which amputation became necessary. In one of these cases it was necessary to amputate within two weeks after the onset of edema. Doubtless the edema itself, has a pernicious effect, acting so as to further impede the circulation of the peripheral parts (in a sort of vicious circle). It is apt to extend rapidly over the whole of the foot, and even up to the ankle and leg.

There seems to be no doubt but that it has a bad influence upon the nutrition of the limb. By compressing the small vessels the compensatory hyperemia is interfered with to a certain extent, and loses much of its efficiency in the nourishment of the parts. A further untoward effect is its inclination to increase the pain, which in these cases is already considerable in the neighborhood of the trophic disturbances.

Pathological examination of the limbs in which marked edema is present shows the absence of involvement of the veins in so many of the cases that these could certainly not be held responsible, although it is possible that

¹ See Briscoe, *Loc. cit.* Chap. VII.

veins proximal to the point of amputation were occluded. Indeed, a satisfactory explanation for its production is difficult to find. It may be regarded as being of inflammatory origin, as the result of a lymphatic inflammation, although a suppurative process is certainly at hand in most of the cases in which it is present.

Persistent Edema the Harbinger of Gangrene.—As already stated, in thrombo-angiitis obliterans continued edema is exceedingly inauspicious. When a manifestation of inevitable gangrene, it may usher in a state of chronic cyanosis of the forepart of the foot, attended with marked coldness and anesthesia, these constituting a group of phenomena characteristic of one form of slowly developing gangrene. It is thus called, since weeks may elapse before the unmistakable and classical external signs of tissue death manifest themselves. The following case will illustrate.

M. K., male, Russian, aged 35 (January 6, 1917), had had an ulcer of one of the toes of the right foot one year previously, and this healed slowly. For six months there were the usual symptoms of intermittent claudication. Following the removal of a callous (?), edema began to develop. This was soon attended with *cyanosis*; these signs with *marked frigidity* and *anesthesia* of the forepart of the foot were the striking and enduring manifestations until amputation was done. None of the usual objective evidences of gangrene appeared during a period of observation from January 6 to January 18. Nevertheless, the pain and the persistent symptoms above mentioned attested to the assumption that the peripheral parts had become gravely compromised. Amputation January 19—Gritti-Stokes operation.

The specimen demonstrated an absence of purulent infiltration or marked necrosis, but an intense ischemia of all the tissues, presaging inevitable tissue death. The popliteal and posterior tibial arteries were completely closed.

CHAPTER XLIX

THROMBO-ANGIITIS OBLITERANS—INTERMITTENT CLAUDICATION

Next to the palpable signs of arterial obliteration, namely, the absence of pulses, this is perhaps one of the most constant features of the disease. In a series of one hundred cases the author obtained a history of its occurrence seventy-eight times in one, forty-eight times in both lower extremities. A story of cramp-like sensations in the calf or in the foot induced by walking, and disappearing when at rest, may precede by weeks, months or years the advent of other phenomena. When associated with vasomotor symptoms, such as coldness, blanching of the foot, with patches of rubor alternating with ischemic areas, or cyanosis, the typical syndrome of Erb is present. However, as elsewhere pointed out, the descriptive appellation *intermittent claudication* is incorrectly applied to this composite complex of sensory plus vasomotor manifestations. The latter often occur in thrombo-angiitis obliterans and other obliterative vascular diseases, unassociated with the typical pains and cramps induced by exertion. We prefer, therefore, to restrict the designation of intermittent claudication to the sensory or sensory-motor signs, acknowledging a certain amount of clinical interdependence of the two varieties. Whilst it is true that exercise may simultaneously evoke

the characteristic pains and vasomotor changes, other excitants such as cold and emotion may bring forth the vasomotor indications alone, unattended by the typical cramps.

In some of the cases there is not only a history of intermittent claudication, but vasomotor and sensory symptoms accompanying. The patients describe one or both feet as becoming suddenly white half way up the foot or as far as the ankle after walking one or two blocks. They experience also a feeling of numbness or a "dead" feeling in the affected foot. There may be no pain in the foot whatsoever, or there may be *pain in the calf*, or the *pain may be altogether absent*. Some say that when they sit down after this change in color, the foot turns red or blue, this being variable whereas the whiteness is a more constant phenomenon. Or, ischemia alone, or "coldness" may be induced by exertion.

Intermittent Claudication with Pulsating Arteries.—Symptoms of intermittent claudication may attend apparently healthy arteries, if we accept the pulsations in the pedal, crural and femoral arteries as a guide. But *one* of the limbs may show advanced obliterative vascular disease, which should be regarded as suggestive of the development of obstructive lesions.

We encounter cases in which one limb gives the symptoms of intermittent claudication for months before the pulses become extinguished. The lesions are probably of limited extent, and involve only the plantar or peroneal arteries that are inaccessible to touch.¹

Vasomotor Symptoms with Intermittent Claudication.—The prevalence of vasomotor manifestations, notably coldness of the foot after walking with numbness and pain in the calf of the leg, in some cases of thrombo-angiitis obliterans has been responsible for much prejudication in the clinician's conception of intermittent claudication. Whilst coldness and pallor of the foot may be accounted for on the basis of obstructive hydrostatic factors alone, wherever intensive degrees of circulatory impediment are present, there are equally marked examples of local ischemia and frigidity due to complicating vasomotor influences. Both exertion and external temperature conditions are influential in the production of pallor and coldness.

It would be erroneous to regard the so-called "intermittent claudication"—pain in the legs and feet on walking with coldness and pallor of the peripheral parts—as a morbid entity. For, it has been well attested and demonstrated by the fact that most exquisite illustrations of such grouping of clinical features are afforded by the disease thrombo-angiitis obliterans. The term intermittent claudication, therefore, should be rejected as descriptive of a disease and restricted to a combination of associated symptoms observable in a number of different pathological processes. To amplify and explain by actual case, the following history may be worthy of study.

Thrombo-angiitis Obliterans with Symptoms of the Sensory and Vasomotor Type of Intermittent Claudication.

A. G., male, Russian, age 33 years, examined November 27, 1908, has been in this country twenty-one years. Smokes six to seven cigarettes a day. He has not been at work for about one year because of trouble with his legs that prevented walking. Illness began three years ago with pain in the sole of the left foot on walking. For two years the pain in the calf of the leg was associated with the other symptoms. He would put his foot into cold water and the pain in the foot would disappear. For two years he did not think it sufficiently severe to consult a physician, until one year ago a physician told him that he had rheumatism, for which he tried baths. *The pain became worse, so that in October, 1907,*

¹ We must not forget that seemingly authentic cases of neurogenic or angioneurotic intermittent claudication have been reported (Westphal, Schlesinger, Oppenheim, Chap. XXVI).

it was so severe that he could not walk at all. He would rub his toes, would suffer for hours with severe pain in the fourth toe and just below the fourth and fifth toes. At that time October, 1907, there was a *little "sore" on the fourth toe.* The pain was always worse at night. His "sore" healed after several weeks. After that he noticed that the foot would get pale and cold, and *later would turn blue and red in the dependent position.* Then last January he went to another physician who gave him fourteen mercury inunctions, *without result.* Then 35 injections of bichloride of mercury and potassium iodide were given *without improvement.* In fact he got worse. *On walking, he says that the instep feels dead, but he has had no pain since the time he had his ulcers last summer.* On walking, his left foot feels peculiar: the ball of his foot falls asleep and he is not able to walk more than six or seven blocks without stopping. After resting, "circulation returns" he thinks. No more sores have developed. *Now his foot turns pale when he goes out and when he takes his shoe off he finds his foot white. Then, if exposed, the color returns.* He feels better in warm weather.

Chief complaint: Coldness of the left foot, and inability to walk because the foot becomes numb.

Physical examination: The right dorsalis pedis does not pulsate; the posterior tibial and popliteal are present. The left dorsalis pedis is absent; the posterior tibial and popliteal are good.

December 1, 1908: Thrombosis of veins of both legs, involving the territory of the internal saphenous, is present. The patient states that his left leg gives him more trouble than the right.

Physical examination: The right dorsalis pedis is absent; the posterior tibial and popliteal pulses are present. The left dorsalis pedis and posterior tibial are absent; the popliteal is present.

The left foot shows moderate erythromelia in the dependent position. The angle of circulatory sufficiency is about 110° .

Résumé: A case of temporary recovery, the left side being more involved than the right, with both popliteals pulsating, and with a history of thromboses of the superficial veins on both sides, probably involving tributaries of the internal saphenous veins.

February 27, 1909, physical examination: Both feet are *cold* to the touch. He says that his feet are always *numb*; he cannot work. No changes in the pulse on the right side are perceptible. The left dorsal pedis and posterior tibial are absent; the popliteal pulse is doubtful or faint.

April 27, 1909: Patient says his *left* foot gets *white* at the instep as soon as he walks a few blocks and the foot feels dead. Has no pain. When he sits down it turns blue. The right foot is somewhat better, but also troubles him in the same way. He also has pain in the back of the left knee. Upon examination the left foot is cold to the touch, the right only slightly cold.

On allowing the feet to hang down for 5 minutes the left becomes dusky, the right slightly blue, but there is no intense cyanosis. A peculiar brown pigmentation of the skin of the extremities masks the real color. At times the left foot shows a slight degree of erythromelia. No evidence of trophic disorder.

Summary: Obliteration of dorsalis pedis of both legs; with posterior tibial on the left, with numbness and coldness as chief symptoms. No trophic disturbances.

October 21, 1909, complains of coldness of feet and he says they get stiff.

Physical examination: Both feet are cold to the touch, the left more than the right.

December 8, 1909: He complains mostly of coldness of both feet and both feet become "dead" when he walks. The right foot troubles him now. He has had no sores.

Physical examination: In dependent position, the left foot takes a dusky reddish purple hue, the right also shows some slight *cyanosis*, with a tinge of red, the color extending a short distance up the dorsum of the foot. Both feet are cold. The big toe of the left foot is cyanotic. There seems to be more cyanosis of both feet than at last examination. Cyanosis is more prominent than the redness; probably getting worse.

January 3, 1910: Color of both feet pretty normal. Remarkable change in appearance, probably due to weather. Left, slight erythromelia. Right, still less.

January 15, 1910: Left foot fair amount of erythromelia, and he complains of coldness of foot.

February 20, 1910: Has "no feeling" in the feet. On examination left foot somewhat more dusky than right, but no erythromelia of either. Right big toe somewhat red.

April 3, 1910: He is getting worse. Left foot often gets red. Now it is cold and toes have a reddish and bluish hue. As left is watched changes of color take place. After a few minutes the redness spreads over the dorsum; it is admixed with blue but is not marked. The right does not change color.

October 8, 1911: Still numb legs, "without any feeling." Color of both feet good, left foot much colder than the right. Coldness beginning at the toes and goes up to the ankle

on the left side, only to base of toes on the right side. Dependent position: Right almost normal color, left gets slightly cyanotic and red. Vessels: Right, as at last examination; left, also the popliteal and femoral pulses poor.

November 10, 1911: Does not feel well, feet get cold.

On examination the left foot is slightly cyanotic, and the skin of the toes looks thin. In the dependent position there is no true erythromelia; but slight increase of cyanosis is noticeable on the left and very slight erythromelia.

Summary: Stationary and practically cured case with both dorsalis pedes closed, but one posterior tibial open; and all the vessels higher up seem open. The chief signs are numbness and coldness of the feet, slight cyanosis and very slight erythromelia of the left. A case of thrombo-angiitis obliterans with varied vasomotor phenomena, and intermittent claudication.

CHAPTER L

THROMBO-ANGIITIS OBLITERANS—PAIN

Thrombo-angiitis Obliterans without Pain.—Although *pain* is an almost certain concomitant of the other characteristic manifestations of the disease, it may be absent for a long period, or extensive obliteration of arteries may be wholly divorced of it. And so the author has observed pulseless popliteal, posterior tibial and dorsalis pedis arteries, with ischemia on elevation, reactionary or chronic rubor, without any complaint or even a recollection of the occurrence of pain on the part of the patient. Such are the latent or insidious cases described elsewhere. When two limbs are simultaneously affected, one may be free of pain, the other the seat of excruciating suffering.

Varieties of Pain.—The symptom of pain in thrombo-angiitis obliterans has both diagnostic and prognostic significance. It is present in a variety of different situations, and is occasioned by a number of diverse underlying causes.

The degree of the pain is variable, not only in the stage where it is brought on by walking, but also when initiated by the trophic disorders and gangrene. In some there are distinct remissions with periods of comparative freedom, in others the pain is constant. When it is severe, the patient may sit with his leg bent at the knee holding the foot in his hand in an effort to obtain relief.

Pain may be so mild as to be a negligible component of the syndrome. Or, it may be so distressing that the usual deterrent forces residing in the ego and preventing us from stepping outside of the bounds of propriety are nullified or put into abeyance. When this occurs the patient falls a victim to psychoses, or his mentality becomes almost completely unbalanced, (see Mental Symptoms). The pain is clinically diversified as follows.

1. Pain of intermittent claudication.
2. Pain of acute thrombo-angiitis obliterans.
 - (a) In the superficial veins (migratory phlebitis).
 - (b) In the deep vessels (acute stage of thrombo-angiitis).
3. Pain with changing position.
4. Pain of ischemia.
5. Pain with chronic cyanosis and erythromelia.
6. Continuous pain antedating gangrene or trophic lesions.
7. Pain with trophic disorders (fissures, ulcers, etc.).
8. Pain with infection.
9. Pain with gangrene.

The *pain* may vary in situation, character, intensity, and relation to movement and posture. Perhaps the most common is that already described under *Intermittent Claudication* as a cramp-like and lancinating pain, or as an ache in the calf, ankle, or throughout the leg. Besides this, however, there are: (1) The vague deep seated pain attending the acute involvement of the deeper vessels; (2) the local and diffuse pain of complicating migrating phlebitis; (3) the pain associated with trophic disorders or gangrene.

We have already referred elsewhere to that vague ache or pain which we may attribute to the acute involvement of the deep seated vessels. To what extent the pain originates in the vessel walls and how much the implication of contiguous nerve is responsible, is difficult to determine. Peculiar "drawing" and aching sensations are described in the calf as occurring independent of locomotion, and may be the premonitory signs of serious, thrombotic invasion of the arteries. Sometimes these are of paroxysmal nature, lasting for several hours (1-4), of spontaneous advent, independent of motion and associated with tenderness to deep pressure. Such sensory phenomena are attributable to migrating thrombotic lesions in the deep vessels; they are not of ischemic or angiospastic nature.

Although the origin of the local pain of acute migrating phlebitis is usually easy to recognize, the lesion may be so extensive¹ that the resultant pain becomes correspondingly diffuse, ache-like and in part indistinguishable from that which emanates from the deeper vessels.

But it is especially when any defect in the skin or infection occurs, that a severe pain in the affected region (though not altogether confined to this) may arise, persist and increase in intensity in a manner quite disproportionate to the size of the lesion. A tiny fissure—one that usually is slow in healing—often suffices to give the patient sleepless nights. Small, insignificant ulcers are frequently so excruciatingly sensitive and painful that until this observation is oft repeated in our clinical work, we are at a loss to reconcile the objective and subjective manifestations. Indeed, occasionally a patient will request amputation of a limb even though the indolent non-healing ulcer has in no sense objectively compromised the integrity of the part. And furthermore, even after amputation of the leg there are many instances in which the pain may persist for days, or even two to three weeks, or more. The development of this condition of intense hyperesthesia may be coincident with functional derangements in the centripetal sensory paths, possibly in the cord itself, that persist even after the original afferent impulses have ceased. Strange to say, however, the infiltration of the posterior tibial nerve behind the malleolus may cause the pain to disappear in some cases; but this is not true for all. It is also noteworthy that vasomotor phenomena not uncommonly appear with or after the advent of the pain, seemingly in some reciprocal relationship. As to whether the continuous sensory impulses are at all responsible for the creation of vasolability through 'higher centers' is a matter worthy of further study.

The pain of intermittent claudication is described in detail under the chapter on Intermittent Claudication. Attention is called here merely to the method of differentiating this symptom from similar and coincident pain due to other causes. When a patient who has discomfort, cramps or pain "throughout the leg" or in the calf or ankle, or on walking, but also has had acute attacks of pain independent of locomotion, the latter may under certain circumstances be referable to recent active thrombosis in some of the deep vascular territories of the leg.

¹ See fulminating cases, Chap. LVIII on Migrating Phlebitis.

The *pendent position* frequently intensifies the pain in the leg and foot, and is described in some instances as coming on as soon as the patient gets out of bed.

Because of conflicting statements, it is often difficult to draw definite conclusions as to the influence of position. The history may reveal in the case of one limb that the pain is increased in the pendent position and aggravated by elevation in the case of the other.

Sequence of Various Types of Pain.—Most commonly a period of intermittent claudication antedates the intense, more delimited pain. Such a stage is often treated as “rheumatism” without relief to the patient. Then follows a period of constantly increasing pain in one or more toes, which may be designated as a *tropho-prodromal*¹ sign, since it usually forecasts the advent of fissures, bullæ or other trophic lesions and even gangrene. With the onset of such lesions a marked increase in the intensity of the suffering can be expected, the latter diminishing and even disappearing with the healing of open wounds. Just prior to or after the cicatrization of such lesions there may be a stage of vasomotor derangement. At this time coldness, pallor and numbness, with their attendant discomforts, may modify the sensations described as “pain” by the patient.

Continuous Pain in Toes.—When the patient begins to complain of continuous distress and then of pain in one or more toes, the disease is usually well developed, and the trophic type of lesions or even gangrene is to be expected. Change in color of the affected toes to a distinct or angry red in the pendent or horizontal position is then also noted by the patient, except in those more uncommon cases where the vasomotor blanching seems to dominate in the clinical picture. A good illustration of the advent of the constant type of pain is offered by the following case.

S. W., male, aged 37, began having pain in calf of left leg when walking but short distance 2½ years ago. A year and a half ago continuous pain in the left big toe set in, which subsequently spread to the second, third and fourth toes. In spite of a 4 week stay at a hospital, the symptoms did not subside.

Seven weeks ago the same pain previously described in the left leg appeared in the right leg, associated with discoloration of the toes and severe pain in the fifth toe. A fissure appeared on the fifth toe because of which the nail was removed.

Four weeks ago the tip of the left big toe became very painful, a bleb appeared which subsequently apparently healed, leaving the region of the nail very painful.

Physical examination: In the horizontal position the forepart of the left leg shows moderate erythromelia, and there is moderate hyperemia over the greater part of the dorsum. The big toe is swollen particularly over the outer part of its distal phalanx, and there is an accumulation of serum under the nail.

In the horizontal position the right foot shows slight erythromelia. The fifth toe is slightly swollen, and presents a fissure on its plantar aspect where the nail was removed.

In the dependent position both feet soon become angry red. In the elevated position the color leaves the big toe of the left foot first, this toe becoming completely blanched within a few seconds. Cyanotic patches are apparent over the second and third left toes, and rapid blanching of the entire foot, with the exception of the cyanotic patches previously described, takes place. The right foot, too, shows marked blanching in this position. The patient complains of severe pain when the legs are elevated.

The external iliac and femoral arteries of both lower extremities pulsate; the right popliteal is present, the left absent as also both posterior tibials and dorsalis pedes.

Tenderness.—This would seem to be an almost inexplicable phenomenon in many cases and at certain stages of the disease. In its most exquisite form it accompanies trophic disorders of rather limited extent, when these manifest themselves as ulcers or deep fissures near the tip of the toe, especially near or at the nail bed.

¹ The word is coined to denote that which is a harbinger of trophic disturbances.

Its existence bespeaks the presence of one of the following conditions: (1) migrating phlebitis; (2) the acute involvement of the deep vessels (deep tenderness); (3) chronic cyanosis, or more or less chronic ischemia of the toe whose nourishment is most impaired (impending or imminent gangrene); (4) trophic lesions (fissures and ulcers); and (5) gangrene.

CHAPTER LI

THROMBO-ANGIITIS OBLITERANS—COLDNESS¹

Coldness of one or more toes or fingers is a common complaint, and, according to the anamneses and records of physical examination, its advent is influenced by a number of different factors. These are exposure to cold or inclement weather, washing in cold water, walking, and more rarely, emotional strain (vasomotor) frequently described by the patient as "excitement."

Just as in the case of the ischemia, rubor and cyanosis, so also here subjective and even objective diminution of temperature is produced either by (A) neurotic (vasomotor) causes, or (B) by abnormal mechanical or hydrostatic agencies.

A. Neurotic Types. (1) *Transitory Vasomotor Coldness*.—After a prodromal stage of intermittent claudication, "coldness and numbness" of one or both feet may be the striking features in the clinical picture. When provoked by walking there ensues the syndrome dignified into a morbid entity by Erb. If the sensory and vasomotor symptoms—that is, the cramps, pains, the pallor and coldness of the parts be alone taken into consideration, "intermittent claudication" will be diagnosticated, whilst, in truth, we will have at hand manifestations of a pathological and clinical unity—thrombo-angiitis obliterans.²

(2) *Prolonged Vasomotor and Hydrostatic Coldness (with Ischemia)*.—When coldness with or without ischemia in the horizontal position is protracted, we are dealing with a stage in which vasomotor influences exert a prolonged effect on the superficial capillaries and arterioles—an influence quite out of proportion in intensity to the degree of organic circulatory interference. Thus, when a patient complains that the toes and foot have been cold (and possibly white) for some time, although not through twenty-four hours of the day, and the sensation is regularly evoked by the horizontal posture as also by exposure to cold, we must differentiate between coldness and pallor due to hydrostatic influences alone—lack of adequate distribution of blood—and that partially motivated by vasomotor activities. Because clinical and pathological observations have shown that coldness and pallor in the horizontal do not go hand in hand, in a given case, with the extent of intravascular obstruction, but that both manifestations may disappear as more and more arterial territory becomes obturated, *the rôle and significance of complicating and associated neurotic agencies becomes clear and comprehensible.*

¹ Because of the intimate association of coldness and ischemia, the description of these two manifestations must needs overlap, so that the two chapters are best studied together.

² For an excellent illustration of the symptoms here mentioned refer to Chap. XLIX, Intermittent Claudication; also see Chap. XXVI.

We assume that by virtue of an excessive lability of the vasomotor mechanism in some cases, the partial circulatory depletion (partial ischemia) occasioned by elevation of the limb to the horizontal is sufficient to elicit disproportionate vasoconstricting response, extending to and implicating particularly the superficial capillaries and arterioles. We have contended and attempted to explain elsewhere¹ that a neurotic reaction is induced by raising the leg ninety degrees above the horizontal.

So, by a combination of two wholly diverse mechanisms, subjective and objective phenomena described as "coldness and whiteness or pallor" are brought into being.

When coldness and pallor occupy but a relatively short period of the clinical history and vanish either completely or in part with progressive aggravation of the pathologic lesions, we are justified in assuming other than merely obstructive agencies as responsible.

It is well, therefore, to attempt to differentiate in making a physical examination between the rôle of mere elevation of the extremity, or insufficient blood supply from the vasomotor influences. Such power of appraisal can be gained by experience.

Another set of hypotheses may be applicable here, too, as previously offered in explanation of other vasomotor phenomena; namely, the local influence of *metabolites*,² (or possibly specific vessel toxins), and the inherent independent functional activity of the capillaries and venules themselves.³ If such additional factors be accepted, it is clear that the regulation of the peripheral circulation in the extremities (as also in organs) is necessarily exceedingly complicated and not always divisible into its several causal influences.

B. Coldness Directly Attributable to Vascular Occlusion.—This, too, may be subjectively or objectively demonstrable. The variations in normal susceptibility to the feeling of "cold" of the extremities, in individuals whose cardiac and vascular systems are apparently normal, is a matter of common—knowledge. So here, too, the neurogenic and emotional factors cannot be excluded and their presence may obscure an otherwise clear reciprocity between arterial disease and thermic conditions. A certain restraint, therefore, must be exercised in the interpretation of "coldness" both of subjective and objective varieties. Some patients with but limited invasion of arterial territories describe "coldness" as an annoying and persisting complaint; whilst others rarely notice it—except under special climatic conditions—even though the arteries are extensively compromised. Where a limited part of the foot, such as one or more toes, are continuously cold, often painfully so, over a protracted period, and objective signs correspond, the phenomenon is of grave import and often initiates a trophic disorder or gangrenous lesion.

Although a certain degree of coldness is common to most of the cases, there is a kind of frigidity that accompanies the severe types of gangrene. In some of these cases where sudden and extensive gangrene may take place, not only the foot, but also a quarter, a third, or a half of the leg will be intensely cold, so that we almost fear that an occlusive thrombosis has occurred.

Objectively we should examine all cases of suspected organic obstructive vascular disease of the extremities by a comparative method of palpation, both as to differences in the warmth of the corresponding extremity, and in

¹ Chaps. XLV and LIV.

² Chap. VII.

³ See Chaps. CVII and CVIII; also group 5, p. 578.

the temperature at different levels. It is a good procedure to pass the palm of the examining hand slowly from the knee (first in front, then behind) towards the foot, noting the degree of warmth or cold, and the upper limit of the zone of frigidity, if such be present. Then each toe should be separately tested and compared with the others of the same foot as well as with those of the other foot.

Perhaps one of the most valuable objective methods of roughly appraising the quantitative influx of blood into the lower extremities, is a *search for this level of distinct lowering of temperature*. To this end, we first eliminate those factors that may lead to fallacious interpretation, to wit: the effects of immediately prior exposure to cold and vasomotor instability. Then, by passing the warm palm of the observer's hand in close contact with the extremity from above downward, and by a comparison with the other side, changes as well as definite coldness at certain levels will be appreciated. Similar methods are applicable to the upper extremity.

As a test for the response of the circulation to special circumstances, such as exercise, thermic influences, etc., the search for the degree and level of coldness is also of some value. Single observations, however, must be discarded as insufficient and unreliable; repeated ones may throw some light on the prognosis.

CHAPTER LII

THROMBO-ANGIITIS OBLITERANS—ARTERIAL PULSATION

A. Absent Pulses.—As an indication of organic arterial disease, a lack of beat in the dorsalis pedis, posterior tibial, popliteal, and femoral arteries is a most reliable sign. In thrombo-angiitis obliterans, a malady that usually comes to our notice after advanced inroads on the integrity of the arterial and even venous distribution of the extremities have occurred, an absence of at least the dorsalis pedis and posterior tibial pulses is to be expected. The occlusion begins for the most part in the peripheral arteries, in the plantars, dorsalis pedis and their larger branches, and it is not long ere the expansile activities of these vessels cease. However, the variations in the intensity and site of the pathological alterations are sufficiently great to make us cognizant of the incidence of a stage or clinical period in which no tangible evidence of arterial obliteration is at hand.

Arterial Pulsation in Certain Early Cases.—Although we must concede the diagnostic value of lack of pulsation in thrombo-angiitis obliterans, normal arterial beats are demonstrable even in the peripheral vessels (that is, dorsalis pedis and posterior tibial) in some of the "early" cases. It is not only theoretically possible, but has been proven beyond peradventure by clinical and pathological observations, that a number of the other characteristic objective phenomena of thrombo-angiitis obliterans may antedate by weeks or months the disappearance of either the dorsalis pedis or posterior tibial pulses. Thus the following sequence of events in a certain case will illustrate.

(1) At the first examination the vessels are found pulsating; ischemia and erythromelia absent.

(2) A period of pain in the calf of the leg with tenderness and some cyanosis in the pendent position, the vessels still pulsating.

(3) The development of marked ischemia on elevation, pain persisting, and still no change in the pulses.

(4) Finally, the disappearance of the pulses.

Again, in other early cases, with the accessible arteries beating, the absence of corresponding pulsations in the other leg, with other symptoms, should arouse our diagnostic suspicions. Or, the existence of a solitary sign, such as ischemia on elevation with or without a history of intermittent claudication or migrating phlebitis, is incontrovertible evidence of the advent of further trouble and of the coincident involvement of arteries beyond the pale of examination by palpation. If we follow carefully the clinical course of such early cases, we will note a progressive disappearance of the pulses, usually in the following sequence—the dorsalis pedis, then the posterior tibial, and then the popliteal. In what period of time this may occur is illustrated by the following case.

H. R., age 32, Russian Hebrew, first examined by the author on August 17, 1908, had had pain in the toes of the left foot 5 years previously; then cramps in the legs up to the knees on walking, over most of the subsequent period. A few weeks before examination he was treated for "phlebitis" of the right leg, that had existed for almost 5 months.

August 17, 1908, right leg: *All the vessels pulsate* but vasomotor phenomena are present as also ischemia on elevation. The left leg shows absence of pulses in the dorsalis pedis and posterior tibial, marked erythromelia, ischemia on elevation—a typical example of thrombo-angiitis obliterans.

December 1, 1908, persisting vasomotor phenomena in the right leg—*vessels still pulsate*.

February and March, 1908, *the dorsalis pedis and posterior tibial arteries of the right foot no longer pulsate*. Left foot—beginning trophic disorder of the big toe; gangrene to be expected.

March 1, 1909, amputation of the left leg.

June, 1909, marked disturbances in the right foot on allowing weight to rest on it, and burning pain in the foot when he walks a short distance with the aid of crutches (thus the typical thrombo-angiitis obliterans symptoms are now well developed in the right leg appearing *pari passu* with the extension of the obliterative process as estimated by investigation of the pulses).

In this instance the disappearance of the dorsalis pedis and posterior tibial pulses within a period of 7 months was coincidental with the transformation of a case of *exquisite vasomotor symptoms*, into one with the usual attributes of true thrombo-angiitis obliterans. Other signs, however, synchronous with the neurotic manifestations, made the diagnosis of organic arterial occlusion acceptable, even at the first examination.

Pulsation Absent in All Arteries of a Limb.—While it is tempting to prognosticate a severe clinical course when arterial occlusion over vast extent is objectively demonstrable, experience teaches that *symptoms may be absent or slight, with obturation of all the accessible vessels of the lower extremities*¹ including the external iliac artery.² So we note a group which may be described under the above caption. Here belong:

(a) Cases without symptoms.

(b) Cases with minimal or insignificant symptoms.

(c) Cases with one or both limbs compromised early and lost.

(a) *Cases without symptoms*, demonstrate the insidious onset and develop-

¹For brevity the words "of the extremity" being implied and self-understood, are frequently omitted in the text.

²It may be recalled here that absent or imperceptible pulsations are not, accurately speaking, identical with obturated vessels (Chap. XXIV).

ment of the disease and the apparent unimportance of multiple pulseless vessels. Such cases, however, are rare and are candidates, as it were, for immediate conversion of a dormant into an intensely active and severe clinical course upon the least insult. An instance of this type has been recounted in Chap. XLII, p. 220.

(b) *Cases with Insignificant Symptoms.*—The absence of many pulses does not imply that we are more apt to find trophic derangements. Indeed, where there is a paucity of manifestations extensive arterial obliteration is one of the striking features in thrombo-angiitis obliterans, as well as in arteriosclerosis. Many of the "latent cases" and those examples where only one of two affected lower extremities is complained of, evidence lack of pulsation in both arteries of the foot, in the popliteal or even the femoral. Where clinical proofs of disease are apparent, these may be minimal, often represented merely by intermittent claudication, frigidity of the foot in cold weather, possibly with attendant attacks of migrating phlebitis; but trophic derangements and gangrene may be absent. The following excerpt from an illustrative case merits brief citation.

Obliterated dorsalis pedis, posterior tibial, popliteal and femoral arteries without trophic disorders.

A. G., 42 years of age, Austrian Hebrew, on February 12, 1909 gives a history of having had trouble in the right foot and leg for about 22 years, difficulty on walking and pain. Until 1 year ago, however, this was not sufficient to give him any concern; but for the last 11 months the pain has been so marked over the inner side of the ankle after walking, that he is trying to obtain relief by means of arch supporters. In addition he has noticed nodules in the skin. Six weeks ago such a red nodule appeared under the skin at about the middle of the right leg. He can go no farther than 1 or 2 blocks at a time.

Physical examination: The right leg is distinctly paler than the left, but there is no chronic erythromelia. All the vessels of the left leg pulsate. On the right side, however, the dorsalis pedis, posterior tibial, popliteal and femoral arteries do not pulsate; the external iliac beat is only faint. On elevation the right leg blanches distinctly.

During December, 1909, and January, 1910, while under observation, he had recurrent attacks of migrating phlebitis involving the region of the right calf and the inner side of the ankle.

A typical case, then, of thrombo-angiitis obliterans combined with migrating phlebitis, and *without any trophic disturbances* in spite of the very extensive vascular occlusion, all of the usual pulses being imperceptible, except a very faint beat in the external iliac artery.

On close observation of many cases with perceptible beats in certain or all of the usual situations, the advent of extinction of the pulse can be demonstrated.

H. R. showed an absence of the posterior tibial and dorsalis pedis pulses of the left leg (the limb more markedly affected), whereas the same vessels of the right leg were beating strongly (August, 1908). In December, 1908, the dorsalis pedis beat of the right foot could no longer be elicited. Later in the month the posterior tibial pulse was also absent. In June, 1909, the popliteal, too, became imperceptible. Therefore, within 1 year (about 10 months) all three pulses, posterior tibial, popliteal and dorsalis pedis disappeared in the right limb.

Intermittent claudication and possibly a "sore" over one toe which may heal, may be the only manifestations. Thus, the following is an example.

B. B.,¹ aged 34 years, Russian Hebrew, when examined June 17, 1909, gave a typical history of migrating phlebitis with trouble in the right leg for 8 years, and in the left leg for 3 years. For 2 years, intermittent claudication in the left leg had been present, and in January of this year a small sore appeared at the tip of the left big toe. His chief complaint was "trouble" with the other leg, and except for some coldness and numbness of the left foot, this extremity gives him little concern.

¹ See Chap. LVIII, p. 286.

Objectively the signs of thrombo-angiitis obliterans of both lower extremities are striking, and the femoral, popliteal, posterior tibial and dorsalis pedis of the left leg fail to pulsate.

(c) *Cases with One or Both Limbs Compromised Early and Lost.*—It may be called to mind here—for it will be elsewhere described *in extenso* and illustrated by clinical example—that there is an acute fulminating thrombo-arteritis and phlebitis involving the deep vessels, as well as of the superficial.¹ The invasion of a large vascular territory may take place within a brief time, contrary to the general rule.

B. Pulses Present.—Valuable as the positive finding of imperceptible pulse may be, the existence of pulsations throughout all of the usually palpable arteries of the lower extremities may not preclude the presence of thrombo-angiitis obliterans or other obliterative or occlusive vascular affection. *Occlusion of certain vascular territories may escape our diagnostic means of interpretation*; and we must have recourse to other concomitant, complicating signs and complexes for diagnostic conclusions, when the affection is restricted to the confines of these. Such regions are the peroneal, digital, and plantar arteries.

Of the many bizarre pictures that thrombo-angiitis obliterans affords, the following apropos of the above observation, may be cited.

Thrombo-angiitis Obliterans with Pulsating Arteries.

M. R., Russian, male, aged 40, when seen November 24, 1908, stated that 6 years ago he had "rheumatism" of both feet, with pain becoming progressively worse in the toes and most marked in cold weather. The pain was finally alleviated by heat and disappeared until 2 years ago, when it recurred most intensely in the middle toe of the left foot. After the application of a carbolic solution, spontaneous gangrene of this member occurred, necessitating amputation.

Although gangrene of the fourth toe of the right foot presented itself 1 year ago, this disappeared leaving trophic disturbances of the nail. One month ago there were trophic disturbances of the middle toe of the right foot and small toe of the left. He further stated that both feet had been red since 2 years.

Physical examination: Slight cyanosis of the left small toe, amputation of the third, otherwise the left foot appears normal. There is marked cyanosis of all the toes of the right foot, most intense in the third.

Upon elevation, slight ischemia of both feet can be elicited.

In the dependent position there is intense cyanosis of both legs, admixed with patches of red; exquisite pain in this position.

Vessels: Both dorsalis pedes, posterior tibials, and femorals pulsate strongly, the popliteals are weak.

November, 1908, amputation of the right middle toe for gangrene. December 29, 1908, returned to hospital because of gangrene of the left little toe.

Physical examination: Bleb over little toe of left foot, filled with pus, erythromelia of rest of toe; remaining toes normal; no cyanosis in dependent position.

January 4, 1909, disarticulation of left little toe for gangrene.

January 15, outer half of dorsum of left foot slightly reddened.

January 20, still erythromelia of the left foot, no cyanosis in the dependent position, ischemia on elevation.

Evidently since November, 1908, *ischemia on elevation has developed, a significant evidence of organic vascular lesion.*

March 21, 1909, on allowing feet to hang, they soon become cyanotic, the blue discoloration being admixed with patches of erythema; soles of both feet pinkish in color; *all vessels pulsate.*

C. Pulsations Disappearing under Observation.—Were it possible to keep cases confined to bed for many months under daily observation, the manner of invasion of new vascular territories particularly in more or less approachable sites could be well studied, and valuable information acquired. This is particularly true as applied to that portion of the posterior tibial

¹ See p. 372, Case I. L., also p. 291, Case H. H.

artery that pulsates behind the internal tibial malleolus. We shall refer elsewhere to what the histories have conveyed in this matter.

Certain interesting data relative to time and advance of the disease, and to the significance of added vascular involvement in the symptomatology, could be derived from a less continuous but frequent study of cases over long periods of time (several years).

The Severity of the Symptoms Corresponding to Arterial Occlusion.—While this caption emphasizes a truism which is applicable in many cases, it needs qualification in two different senses. For, we have learned firstly, that extensive arterial occlusion may be adequately compensated for by collaterals and have no subjective concomitants (Chap. XLII) and secondly, that the presence of pulsation in certain vessels may be associated with widespread obturation in many distal and concealed channels. Thus, a patent posterior tibial is not significant if the plantar, dorsalis pedis, dorsalis hallucis and possibly also the peroneal arteries are closed.

Importance of the Popliteal Pulse.—The disappearance of the popliteal may correspond to aggravation of symptoms. So, in a case (D. B.) the course may be summarized as follows:

D. B. in 1896, had migrating phlebitis over the left thigh; 1899, phlebitis over right calf.

In 1904, migrating phlebitis in left antecubital region involving the median cephalic vein and one of the anterior ulnar veins. A specimen removed for microscopic examination showed acute inflammatory lesions that were not correctly interpreted at that time, but after subsequent studies by the author, the lesions were recognized as being those of the acute phase of thrombo-angiitis obliterans. At the same time the patient had prodromal pains in the ankle of the left foot with some cyanosis in the pendent position.

In January, 1907, the posterior tibial, and dorsalis pedis arteries of both feet did not beat, both popliteals did.

February, 1907, symptoms, especially referable to the upper extremities were noted, some pain on walking and rubor of the left foot.

In December, 1907, the usual symptoms of thrombo-angiitis obliterans in both legs.

January 3, 1908, both posterior tibials pulseless, both popliteals beat strongly.

February 7, 1908, right popliteal pulse strong; left diminished.

September 7, 1908, right popliteal pulse has disappeared, with this, *distinct aggravation in condition of right leg and more pain.*

November 19, 1908, pulsations the same, left popliteal still present. Up to early in 1908 the left leg was distinctly worse, the right popliteal pulse better than the left. Since then there was marked intensification of symptoms on the right side with absence of the popliteal pulse. In both feet there are rubor and cyanosis with ischemia on elevation.

April to June, 1909—ulcers of both feet; condition of both aggravated and *all of the pulses except the femorals and iliacs, are now absent.*

Almost simultaneous loss of the popliteal pulse with increase in the severity of the symptoms, followed by gangrene and amputation is illustrated by the following case.

S. S., February 5, 1910, migrating phlebitis 1908, 1 year ago intermittent claudication.

February 6, 1910, evident involvement of both lower extremities, dorsalis pedis and posterior tibial arteries pulseless, all others patent.

March 20, 1910, aggravation of condition in both legs.

January 3, 1911, right foot looks somewhat withered, simulating sclerodactyly, a dead patch of skin over the big toe, right popliteal pulse now absent.

January 28, 1911, Gritti-Stokes amputation (right).

Disappearance of Pulses Compatible with Arrested Symptoms.—To conclude that progressive arterial occlusion should correspond with an exaggeration in the extent and degree of the complaints, would be a universally warrantable assumption, were it not for the occurrence of the following two types of clinical complexes, first the dormant obliterative process without subjective signs, and second, the inverse type in which “apparent healing” with cessa-

tion of subjective phenomena or even regression of objective manifestations may take place.

The cases exemplifying the loss of pulsation unattended with subjective and objective alterations perceptible to the patient have been described on p. 220, 6. They seemingly invalidate and nullify the deductions derivable from the presence of pulseless vessels. Our ability to elicit other coincident signs of which the patient is unaware fortifies the diagnostic value of the silent vessels. Such indications elsewhere alluded to, are notably ischemia on elevation, chronic or induced rubor and possibly the demonstration of a diminished angle of circulatory sufficiency.

To illustrate the two opposed dicta, we may cite in brief the salient facts of the following history, showing:

1st, that pulses disappear *pari passu* with progressive sensory and circulatory manifestations; and

2nd, that they are absent while symptoms regress and the latent or arrested stage is being developed.

M. C., aged 24 years, with the usual prodromal symptoms, when examined March 18, 1908, gave these physical signs; left leg in a state of erythromelia, dorsalis pedis absent, all other pulses present; right leg shows doubtful ischemia, all vessels beating.

November, 1909, the left leg "cured" as far as the subjective manifestations are concerned, but *erythromelia persists*; dorsalis pedis pulse absent, posterior tibial very faint.

The right leg now gives him trouble, intermittent claudication and a trophic ulcer over the big toe are present. The dorsalis pedis and the posterior tibial arteries do not beat.

February 12, 1910, under conservative treatment the gangrenous area on the right big toe has practically healed, and the dorsalis pedis and posterior tibial arteries of both legs are pulseless. No symptoms on the left, objectively erythromelia is present.

Epicrisis.—Closure of two vessels of the right, one of the left leg, while under observation, with aggravation of symptoms in the former, improvement in the latter.

Such *antagonistic clinical states* when viewed in relation to advancing vascular obturation, can only signify and emphasize *that the state of the collateral paths plays just as important a rôle in symptomatology as the quantitative circulatory impediment*.

Sequence of Loss of Pulsation.—A careful search for the inception of the occlusive process in the pulsating arteries discloses the following as the usual chronological sequence in loss of beat: first, in the dorsalis pedis, then in the posterior tibial and popliteal, and finally, in the femoral and external iliac artery (the latter being but rarely affected). No inflexible rule, however, is applicable, since the closure of the posterior tibial artery behind the malleolus may antedate loss of pulsation in the dorsalis pedis, an indication, too, of prior and more extensive disease in the plantar distribution.

The advance of the lesion may occur so rapidly that within 1 year or less, all the pulses of one extremity may be missing, although symptoms may be moderate and gangrene absent.

J. A., February 26, 1907, case with intense blanching of the right foot on exposure to cold and on walking, began 1 year before with sudden attack of inability to walk, there being no definite localization of the pain, which was referred to the whole leg (an acute attack of thrombo-angiitis obliterans?). All of the usual vessels of the right leg are pulseless; the big toe is pale, the others slightly cyanotic.

If a patient be kept long enough under observation, the dorsalis pedis or posterior tibial pulses, or both, may be observed to become extinguished. Occasionally, other symptoms such as intermittent claudication may precede the loss of certain pulses. For, intermittent claudication may depend on the closure of deep arteries beyond the realm of diagnostic palpation.

Intermittent claudication may appear before the advent of erythromelia. The following case will illustrate:—

F. K., Russian Hebrew, 24 years of age, November 5, 1907, had evidently been troubled mostly with the big toe of the left foot; and amputation became necessary. There was, however, a distinct history of pain in the right calf. On physical examination the right dorsalis pedis pulse was distinctly palpable, although the left was not palpable. May 27, 1908, the beat in the dorsalis pedis of the right leg disappeared. The intermittent claudication antedated the disappearance of the pulses by a considerable period.

Relation of Pulsation and Clinical Duration.—So capricious are the exacerbations of this disease, that no conclusions as to the age of the process should be drawn from mere clinical observations alone. The extremity affected for many years may show fewer pulseless vessels, and be in better condition than the other in which symptoms have been noted but recently.

B. B., after symptoms in the right leg for 8 years, with the left implicated for 3 years, demonstrated clinically a more extensive disease of the latter when *none* of the pulses could be elicited, while a good femoral beat was present in the other extremity. The other objective and physical phenomena, too, gave testimony to the more grave vascular impairment of the left in a smaller angle of circulatory sufficiency and more marked ischemia.

Pulsation and the Angle of Circulatory Sufficiency.—The number of pulsating vessels is not always in harmony with adequacy of circulation, nor is it in consonance with the angle of circulatory sufficiency. Thus, this may be less than 90° —and evidence of marked impairment—and still the popliteal and other arteries may be pulsating. In other patients, however, where we find both legs involved, the palpable extent of vascular obliteration corresponds fairly well with the intensity of the other signs. So, erythromelia and ischemia may be most marked on the side where all three vessels of the leg and foot are found pulseless. In one case (B. H.) 3 vessels were pulseless on the left side and 2 on the right, with a corresponding development of the symptoms.

D. Pulses of the Upper Extremities.—A more detailed record of the involvement of the radial and ulnar arteries will be found in the chapter on the Upper Extremities in Thrombo-angiitis Obliterans. Here we will simply allude to certain peculiarities in the relationship between evidences of arterial obturation and symptomatology.

The *radial* pulse may vanish during the period of clinical observation without any other clinical signs referable to such closure.¹

The radial pulse may become extinct simultaneously with the manifestation of an acute thrombo-arteritis and periarteritis; but there may be no other symptoms save those referable to the local alteration in the recently occluded and inflamed vessel.

Vasomotor symptoms may antedate the disappearance of the radial pulse, in which case differentiation from the vasomotor neuroses may be difficult or almost impossible. The unilateral appearance (asymmetrical) of the affection speaks in favor of thrombo-angiitis obliterans.

A further discussion of this phase of the subject will be found in Chap. LIX.

E. Return of Pulsation.—Observers report return of pulsation in arteries that had been seemingly obstructed; and, in personal communications from clinicians, this fact has been made note of. That pulsation cannot return in an artery, that is completely closed through the lesions of thrombo-angiitis obliterans, we are convinced from the pathological changes. However,

¹ Case J. A., p. 295.

dissection of numerous amputated limbs has given a clue as to the possible cause of the reported reestablishment of the dorsalis pedis and anterior tibial pulses, and it is these vessels in which the observation has been most frequently made. A glance at Figs. 47 and 56c will demonstrate how

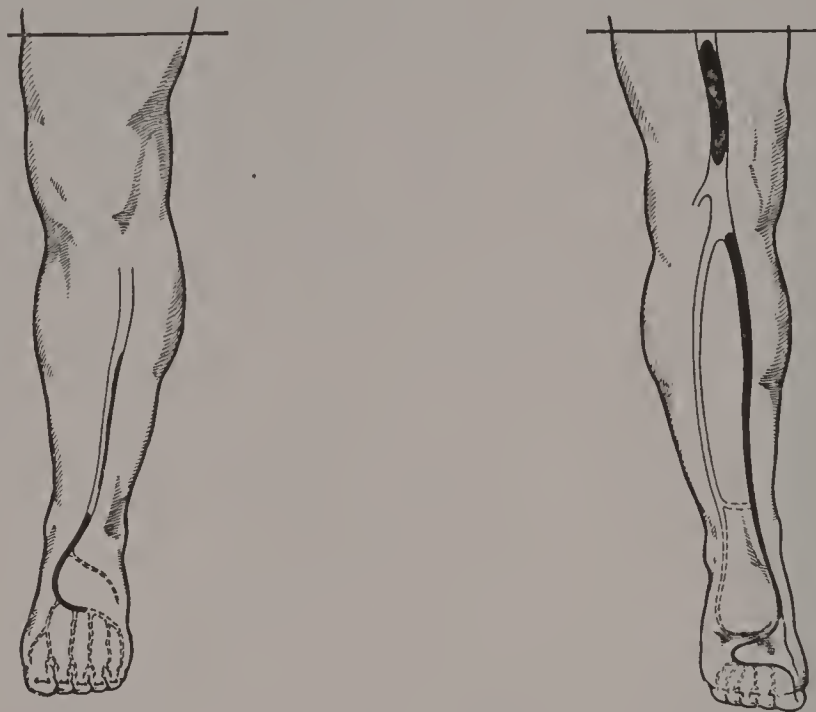


FIG. 47.—Representation of the patency of certain vascular territories in thrombo-angiitis obliterans, and its possible effect on the perceptibility of the pulses.

sections of the anterior tibial or dorsalis pedis artery in their palpable portions may remain patent, whilst the central more proximal parts may be partly or completely occluded. In such cases the artery is more or less collapsed, or allows a small amount of blood to trickle through, or the circulatory force therein is insufficient to produce a beat. With increasing and improving circulation through collateral paths, pulsation may become reestablished, the blood flowing through devious channels in uninvolved territory.

CHAPTER LIII

THROMBO-ANGIITIS OBLITERANS—MENTAL SYMPTOMS

The gloomy outlook in this malady has become so well known to a certain class of the population in many of our¹ big cities, that the dread of the consequences surpasses even the fear of the necessary attendant endurances. Thus, amongst the more highly educated (including physicians), temporary neuroses are not uncommon, often aroused by fancied or simulating manifestations in the extremities. When one or the other of the subjective symptoms of thrombo-angiitis obliterans persists, and when no adequate causal explanation is forthcoming, even in the absence of closed vessels or the characteristic objective signs, we should regard the case as a suspect, although allaying the patient's apprehensions as much as we can.

The patients who have run the gamut of many distressing lesions, severe intermittent claudication, exceedingly painful toes with or without ischemia

¹ United States.

or cyanosis, severe and even excruciating local pain, associated with fissures, ulcers and gangrene, with inability to walk, possibly with the experience of single or multiple amputations of parts of one or more limbs—in these it is not surprising that with increasing calamitous happenings and constant attention to their ills, the afflicted should retire into their subjective world, where the intolerability of their own physical status is paramount.

A haggard look, the staring eyes, the trunk bent with arms clasping and embracing the knee and leg of the affected part, is a striking and well known picture. Or, the foot is held tenaciously, the sole or dorsum rubbed and stroked in fruitless unavailing attempts to mitigate the intensity of the pain.

So distressing can the symptoms be, that it is little wonder that intense mental depression is common. The pain, the disability, the threat of gangrene aroused by a knowledge of the fate of fellows in distress, so pervades every thought and action of certain cases as to cause complete demoralization, and in a few instances has led to attempts at suicide. One of the author's cases successfully accomplished this with illuminating gas; another cut his throat with a razor whilst in the hospital, the enormous gash miraculously avoiding the jugulars.

The author had just made rounds, was called back and was able to save the patient by immediate suture of the parts, including the transversely cut larynx, and by the introduction of a tracheotomy tube.

CHAPTER LIV

THROMBO-ANGIITIS OBLITERANS—VASOMOTOR SYMPTOMS

What with the perplexing nature of the fleeting pains of the prodromal acute stage, what with the long doubtful period of intermittent claudication that is so often underestimated or regarded as "rheumatic" or orthostatic, and, what with the confusing objective phenomena due to nervous agencies, it is little wonder that thrombo-angiitis obliterans is so often mistaken for other maladies. The attendant vasomotor disturbances, especially when such objectively dominate the clinical picture, may add no negligible onus to the clinician's diagnostic task. Although in thrombo-angiitis obliterans the paroxysmal nature of such symptoms is less marked or absent, the coexistence of other neuroses less frequent, the response to emotional influences not so striking, there still remain sufficient points of resemblance to account for the difficulties of differentiation.

Vasomotor phenomena may occur independently, unaccompanied by the usual hydrostatic and mechanical color changes, at a time when even the vessels pulsate, may be superimposed, as it were, or be a coincidental manifestation in a well developed clinical picture of this disease. Both upper and lower extremities may be affected.

It is in the cases of involvement of both lower extremities but with vasomotor disturbances confined to one of them, that opportunity for comparative study of the confusing phenomena is afforded. The limb in the more advanced stage is usually indubitably stigmatized as the seat of arterial occlusion by the *ischemia* on elevation, chronic *erythromelia* and *pulseless vessels*. The other limb may be markedly *blanched* even in the pendent posi-

tion—an evidence of vasomotor influence. Such pallor may give way to intense *cyanosis* admixed with areas of an ashen color in which vestiges of blanching can be discerned. *No rubor* develops in this position of the limb. The blanching and cyanosis are *independent of posture*. Persistent syncope of short duration followed by cyanosis, uninfluenced by position is one of the characteristic types of vasomotor derangement.

Walking and *cold* exert a distinct influence in the incitement of neurotic vascular manifestations, and the phenomena thus brought forth, have, when coupled with the “cramps and pains” in the legs, been described by Erb and designated as “intermittent claudication.” We have alluded elsewhere to the advantages of segregating the sensory¹ group—which we shall call symptoms of “intermittent claudication”—from that of vasomotor instability, since the two are not necessarily interrelated, mutually dependent nor coexistent.

Referring, here, only to the vasomotor symptoms, it must be recorded that transitory or even prolonged syncope may result from either walking or exposure to cold in a given case, or from either one of these instrumentalities alone. A striking pallor may persist in the pendent position offering a marked contrast to the usual hyperemia in this posture, or to the other leg if that is also the seat of the malady. The blanching may occupy the whole or part of the foot, may spare some of the toes and may be associated with patches of cyanosis, the affected area usually presenting a distinct reduction in temperature.

Patients at times will notice very early in the disease that the foot changes color. They will say that it has a tendency to become pale in cold weather and remain so; in the dependent position, they complain of marked redness and often blueness, and at times of coldness. This is a rather constant description in many of the histories. Very often these manifestations give way to the development of intense local pain in one of the toes with the subsequent appearance of trophic disturbances. Again in some cases, irrespective of temperature conditions, syncope and coldness seem to be brought forth on exertion or merely on locomotion, the story being “when I go out my foot becomes pale; when I take my shoe off, I find it has turned white.” To illustrate by a case:

M. N. examined November 24, 1914. The right foot is very pale, even in the pendent position, except for the little toe which is red. When he walks, he says the little toe also becomes white. On pressing the toes, the tips become cyanotic. The foot is very cold; there are no ulcers and no edema.

After walking about for a while the right foot again shows signs of vasomotor disturbance, but instead of pallor there is a mottling of red and white, there being patches of white at the base and over the dorsum of some of the toes, the greater portion of the dorsum of the foot being red. At the same time the plantar surfaces of all the toes have a cadaveric hue. The right dorsalis pedis and posterior tibial are pulseless; left dorsalis pedis absent, but posterior tibial present.

While an abnormal color may repeatedly afford an unchanging picture under similar circumstances, the vasomotor disturbances occasionally exhibit a variegation with kaleidoscopic mottlings of tints of yellowish white, red, purple and blue. Fugitive pallor may yield to a marmorated combination of patches of red and white, these in turn being replaced by cyanotic and pallid areas. Or finally, unless a more or less persistent cyanosis ensue, all play of colors will cease and reactionary rubor will terminate the ephemeral phenomena.

¹ The sensory group has been described in Chap. XLIX on Intermittent Claudication.

Besides the demonstration of one or more pulseless vessels (if such are present), and ischemia on elevation, an important and valuable method for the recognition of the vasomotor symptoms is the possibility of eliciting the phenomenon of reactionary erythromelia. When in doubt, given a case with syncope either of spontaneous or induced advent, or with alternating pallor and cyanosis, or pallor and patches of red, repeated elevation and depression of the leg may dispel all these neurotic displays and produce a distinct and continued rubor in the pendent or even in the horizontal position.

Vasomotor Manifestations May Merely Occupy the Early Clinical Stages of the Malady.—Thus, in reviewing the history of a characteristic case (H. R.) we find that at a time when the left leg showed all the typical symptoms with rubor, the right presented none of these except ischemia on elevation. On the other hand, there were vasomotor symptoms in the latter, namely, cyanosis, a blanched condition of the foot when the shoe was taken off (particularly in cold weather), cyanotic patches at the tips of the toes, and coldness. This complex was observed on several occasions.

Notes taken December 1 1908 read: On taking off the left shoe, the foot is fairly red, the right is slightly blanched, but all the vessels of the right leg pulsate. However, ischemia could be elicited on elevation, an evidence of arterial occlusion.

If we compare the limb exhibiting vasomotor symptoms with the other that is the seat of a more advanced process, we will note that the former is not swollen, the toes not tumefied, rubor absent and the color yellowish white; or, the toes may be markedly blanched, particularly if they have been exposed to cold. In the dependent position, also, a difference is seen in the two limbs. The one that combines the early stage of thrombo-angiitis obliterans with vasomotor symptoms, shows cyanosis after the leg has been hanging down, the distal phalanges or phalanx being of a deep dusky purple; the color may be unmixed with any tinge of red, and the rest of the foot also may show a cyanotic hue; a pale, ashen skin in many places modifies the picture. However, rubor is absent. This condition may change in such a leg, so that when the leg is examined 10 or 11 months later (in the case H. R. 11 months later), the appearance may have completely changed, the usual typical signs, marked erythromelia together with or without cyanosis being in evidence.

A study of the case H. R. threw no light on the reason for the marked vasomotor symptoms in the right leg. They persisted for a long time. They were present August 17, 1908, and even November, 1909, at a time when there developed deep cyanosis of the big toe due to impending gangrene, and the rest of the foot had a slightly bluish color. The dorsum of the foot still exhibited occasional fugitive areas of unexplicable syncope.

Syncope or Ischemia after Exertion.—While the typical picture of intermittent claudication is characterized by the predominance of sensory manifestations sometimes with attendant pallor of the foot and coldness, the vasomotor symptoms may exist alone and be evoked by the same form and degree of exertion as ordinarily excites sensory responses. One limb may be striking because of coldness, the other because of pallor, pain being absent in both. The following case will illustrate.

Thrombo-angiitis Obliterans with Migrating Phlebitis, Syncope and Coldness of the Feet after Exertion.

I. B., Russian, 33 years of age, typical case of thrombo-angiitis obliterans with migrating phlebitis states that the right foot becomes white and cold, sometimes pink after walking. The left foot also becomes cold and tires easily; the pallor of the right foot is striking, the left slightly cyanotic.

Evidences of Altered Vasomotor Function.—Many as are the clinical phenomena illustrative of the peculiar instability of the peripheral vasomotor apparatus, still further evidence thereof is obtainable through simple clinical tests. Vagaries in vasomotor function,¹ it is true, may modify and impair the uniformity of the demonstrable phenomena; nevertheless, certain essentially reliable reactions are wont to follow these motivating factors—(1) elevation of the limb; (2) thermic influences (cold); (3) mechanical irritation (dermatographic reactions); and (4) exercise.

It has already been shown that all of these may evoke not only immediate, but unduly prolonged vasoconstriction of the capillaries and arterioles.

The vasodilating mechanism may be activated on the other hand through such forces as these: Establishment of preliminary ischemia by elevation of the leg with consequent refilling of the peripheral vascular branches in the pendent position (reactionary rubor); temporary compression of the femoral artery (3 to 5 minutes); or application of a constricting bandage at the root of the limb. Less effective means of evoking vasodilatation is the application of external heat and diathermy.

If we examine and compare the healthy and affected lower extremities in the horizontal position, we may demonstrate that where there are obstructed arteries, normal red dermatographic reactions are usually substituted by excessive and persistent pallor; that is, a reversal in the sense of vasoconstriction takes place over an unusually large zone. The test is thus carried out: The femoral artery is compressed for 3 minutes; this is followed by tardy and imperfect fading out of the existing chronic rubor of the foot (vide Chap. XII, p. 84, paradoxical rubor and ischemia). If then a number of scratches be forcibly made over the foot during this period of arrested circulation, and the femoral artery be then released, an abnormal persistence of pallor in and around the irritated zone will be noted. An ischemic area of considerable size will be in striking contrast to the general reactionary and intensive rubor of the rest of the foot.

Quite different will be the reactions of the healthy extremity. Firstly, the ischemia of the foot will be more intensive and of more rapid advent after the artery is compressed. This paradoxical ischemia on the healthy side has been referred to in the Chapter on Collateral Circulation; it is an evidence of the lack of development of substituting by-paths where the arteries are patent. No such dermatographia alba is here evoked; but the scratches soon attain the normal hyperemia.

Such are some of the demonstrable evidence of altered vasomotility in the affected territories. To certain excitants an unusually hypersensitive vasoconstricting mechanism is set into motion; to others, vasodilatation. Amongst the former agents belong depletion and ischemia (consequent upon elevation of the part), cold, mechanical irritation, and exercise. Whatever tends to produce a plenum, however, such as the pendent position, sets the dilating mechanism into activity. The reactionary rubor in the foot after compressing the femoral artery is much more pronounced and of more rapid advent on the side of the obstructed arteries—another sign of altered vasomotility.

In explanation of vasomotor lability may be mentioned Kravkof² on the effect of thrombosis on the vasomotor functions. He states that: "In the coagulation of blood certain protein-forming amines are formed, possessing vasoconstrictor powers, and therefore the vasoconstrictor effect of the serum may be ascribed, not to adrenalin, but to these protein-forming amines."

¹ For vasoneurosis attending arteriosclerotic disease, see p. 578, paragraph 5.

² Oppel, *Gangræna Arteriitica Suprarenalis*, *Lancet*, July 15, 1922, p. 116.

CHAPTER LV

THROMBO-ANGIITIS OBLITERANS—OSSEOUS CHANGES

Rather characteristic of thrombo-angiitis obliterans is the absence of bone absorption of the terminal phalanges. A differential diagnostic point is thus at hand that may serve to distinguish it from Raynaud's disease and sclerodactyly. However, in one case, very marked diffuse bone absorption



FIG. 48.—General rarefaction of the osseous tissue with absence of absorption of the distal ends or terminal phalanges in thrombo-angiitis obliterans.

was noted, involving the lower end of the radius and ulna, all of the carpal bones, the bases of the metacarpal, as well as the shafts of the phalanges. The radiogram is depicted in Fig. 48.¹ Rarefaction of the osseous tissue due to impaired circulation and obliteration of the radial and ulnar arteries was

¹ See section Involvement of the Upper Extremities in Thrombo-angiitis Obliterans (Chap. LIX).

apparently responsible here. But the characteristic disappearance of terminal portions of the phalanges was absent.¹

Secondary destructive osseous alterations, defects, erosions and necroses, may occur as the result of trophic disorders, gangrene and infection. But these are lesions common to other forms of gangrene, and defective circulation plus infection.

A diffuse atrophy of bones due to disuse is also no more pathognomic than those just mentioned; it may be expected in those in whom one or more extremities have been extensively involved or not employed on locomotion for a long time.

A differentiation from the bony changes in the nerve or anesthetic type of lepra will be clarified by a reference to Chap. XIV, p. 94.

CHAPTER LVI

THROMBO-ANGIITIS OBLITERANS—STATISTICAL DATA

Although in the light of more recent experiences certain modifications of the following data may become necessary, they may be taken as indicating average findings in a series of 100 cases collected for special investigation in the year 1916. Over 500 cases have come under the notice of the author, but a careful statistical review has not been made since 1916.

Of 100 consecutive cases reviewed, there were 100 Hebrews; of 400 other cases observed, 10 Gentiles.

There were 76 of Russian birth, 17 of Austrian birth, 3 Americans (of foreign extraction), 2 Roumanians, 1 German, and 1 Turk.

The sex incidence was 99 males, 1 female; among the other 400 cases, however, 2 additional females were studied.

The division of 100 cases in whom there were 171 lower extremities involved was as follows: both lower extremities in 71 cases, the right only in 7 cases, and the left only in 22 cases, the preponderance of the left over the right being noteworthy. In other words, the majority of cases of thrombo-angiitis obliterans, if followed for a sufficiently long period of time, will show the lesion in both lower extremities.

Of the upper extremities, which are less frequently involved, 30 arms were affected in 21 cases; both arms in 9 cases, the right only in 5, and the left only in 7, again demonstrating a slight increase of the left over the right.

The cases with involvement of both upper and lower extremities (21) revealed involvement of both upper and both lower extremities in 8 cases, 2 lower and 1 upper in 10 cases, 2 upper and 1 lower in 1 case, and 1 upper and 1 lower in 2 cases.

Although the age at the onset of the disease varied considerably, ranging from 17 years to 56, the average age was 32 years, 5 months. These figures, however, are much too high, since it is very difficult to estimate the exact age at which the disease began, because of the insidious nature of the onset, and the fact that the onset is overlooked in many cases.

The advent of gangrene, which in some instances ushered in the disease, occurred in others from 1 year and 8 months after the first symptom was

¹ See Chap. XCIX, Raynaud's Disease.

noted, to 12 years after the onset. Amputation was carried out in 52 cases of the 100.

In some cases the gangrene set in within a short time or almost simultaneously with the apparent onset, the longest period being 12 years after the beginning of the complaint.

Doubtless in many of the cases amputation became necessary at some later date, when they were no longer under observation, so that an estimate of 75 per cent or 80 per cent would not be too high.

A similar disease is described as occurring not infrequently amongst the Japanese. Koyano collected 120 cases during the years 1900 to 1921, and gives the following deductions. Most of the cases occur in young males between the ages of 20 and 40, usually in the laboring classes. Inadequate and poor diet,¹ and local exposure to wet and cold are given as factors in etiology. Most of the cases were moderate smokers. The lower extremities were most frequently affected. The pulses were extinct in the following order, dorsalis pedis, anterior and posterior tibial, popliteal, and lastly the femoral. About two-thirds of the cases on admission to the hospital had already lost the right and left popliteal pulses. The blood viscosity was somewhat high, 5.16 in the average case (Koyano); blood sugar normal, as well as cholesterol. The Wassermann test was usually negative. The Japanese laud considerably the hypodermic injections of Ringer's solution (Mayesima-Koga), attributing its efficacy (?) to its power to diminish the viscosity of the blood. The same author was able to find the "acute" lesions in but one case, and therefore is surprised at the relative frequency of the characteristic findings amongst the cases observed in the United States. Evidently the migrating phlebitis was either overlooked or it is rarely associated in the disease of the Japanese.

CHAPTER LVII

THROMBO-ANGIITIS OBLITERANS—ETIOLOGY

The cause of the pathological process in thrombo-angiitis obliterans has not yet been definitely established. By his studies of the clinical aspect and pathology of the disease, the author has established the following facts. That the disease *is not an endarteritis obliterans*; that it is an occlusive thrombotic process involving the deep arteries and veins of the upper and lower extremities, or the superficial veins; that the early stages of the disease manifest themselves in an inflammatory lesion which shows a specific and characteristic morphological picture, while in the process of healing; and that in the early or acute stage, certain purulent foci make their appearance that would suggest a microbial agent or infectious causative factor. No organism, however, has as yet been demonstrated, even in the superficial veins, when these are in the stage of acute inflammation.

Syphilis has been regarded by some as a possible cause, but a study of the histories and of the Wassermann tests in more than 30 cases² has shown that lues is not responsible.

It is a striking circumstance that of a series of 500 cases, the author found only 3 cases in women, and in these patients no amputation was performed, so that the diagnosis was made on clinical signs alone. Furthermore, it is interesting that but 4 cases out of 500 did not belong to the Semitic race.

¹ Some of the more intelligent Russian immigrants have called the author's attention to this factor; but this is irreconcilable with the development of the malady in cases in affluent circumstances since birth.

² Buerger and Kaliski, Med. Rec., Oct. 15, 1910.

Tobacco is probably a predisposing factor, and may be regarded at least as causing some alteration in the vessels that makes them liable to the attacks of inflammation and thrombosis. Most of the cases are heavy smokers, although smoking was denied in 1 per cent of the author's cases.

Here, more especially than in any of the organs or tissues of the body, must we seek not only for predisposing moments, but also for the agency that directly motivates the inflammatory thrombotic lesion. The conducive factor can certainly not be held wholly accountable. Unwarrantable are inferential hypotheses that would attribute an essential rôle to mere contributory forces. It is immaterial whether these be ontogenetic (individualistic traits) or phylogenetic (Hebrew races), acquired (as thermic cold), traumatic (after cutting nail, etc.), inebriant or chemical intoxicants (nicotine, ergot, toxins of typhus).

An understanding of the histological alterations in the vessels could limit the promulgation of hypotheses or etiology that are of purely theoretical nature.

Predisposition to Thrombosis.—If a bland thrombosis without inflammatory process occurred here, we could perhaps have greater confidence in those hypotheses that seek a special thrombophilic tendency in explanation of the extensive obturating process. Although a certain chemical predisposition of the intima or a diminished metabolism in the vascular wall (Zurhelle¹) cannot be excluded from the realm of possibility and may lend to the blood a tendency to clot *in loco*, it is more likely that the determining factor is that sum of chemical and toxic moments that are set into activity *pari passu* with the incidence of the inflammatory lesion.

From time to time most interesting explanations are given by various authors and commentators of the cause of this malady, and often individual predisposing factors are dignified by the appellation "exciting cause." Thus, hyperglycemia, or an increased sugar content of the blood, and dyscrasias of endocrine origin have been suggested as causative factors (W. Meyer). But we must not forget that enough clinical and pathological data are at hand to furnish us with a reliable concept as to what is here actually influential in producing the changes in the vascular system. It is known that the arteries and veins, *par excellence*, furnish examples of tissue complexes requiring several factors for production of pathological alterations. And, strange to say, one or another of these factors (that are merely predisposing agents) are apt to be singled out and heralded as the true cause. When the author's pathological studies revealed that certain specific histological, architectural alterations in the vessels were characteristic of the disease thrombo-angiitis obliterans, it was not presumptuous to conclude that a special exciting agent, be it a toxin or organism, must play a rôle here, in addition to the many other conducive circumstances that may play larger or smaller parts. For how else can we explain the occurrence of the unique or specific alterations that are found nowhere else in thrombotic processes and are a pathognomonic for thrombo-angiitis obliterans, just as the peculiar pathological pictures of tuberculosis are attributable to the tubercle bacillus, and the changes seen in the glands of Hodgkin's disease are doubtless the reactions to special agents.

Reverting to the peculiar reaction of arteries and veins, one may emphasize the fact that more than one factor must be invoked in the case of these peculiar tissue changes. Thus, stasis, locomotion, dependency of the limbs,

¹ Zurhelle, Zentralbl. f. Gynec., 1908, No. 43.

activity of circulation, *vis a tergo*, tobacco, age, sex, and thermal influences—all these play greater or lesser rôles in determining thrombotic and atheromatous occlusion.

As for tobacco, its influence has been recognized for many years. Erb, long ago, in papers written subsequent to his publications on intermittent claudication, attributed extensive atherosclerotic conditions of the lower extremities, in the main, to the influence of *tobacco*. Just how far the absorption of tobacco poisons is responsible for the degenerative changes in the arterial walls cannot be determined accurately, but that it may be safely regarded as a predisposing cause, no one will venture to deny. So also in thrombo-angiitis obliterans, it is possible that the use of tobacco may render the vessels more susceptible to special agents, be they toxic or infectious, but that tobacco is the only and exciting cause is exceedingly doubtful and highly improbable.

Cases of migrating phlebitis in patients who are heavy smokers occur not infrequently. In these, the territory of the saphenous vein becomes gradually occluded, and the differential diagnosis between migrating phlebitis of the "bland type" and migrating phlebitis associated with thrombo-angiitis obliterans must be made. If we excise a portion of the vein in thrombo-phlebitis of the *bland type*, we find, it is true, slight changes in the media, but an occlusive thrombus that presents *none* of the characteristic lesions. In such cases we are dealing with a bland thrombosis in vessels that are damaged by various influences, tobacco, or other causes. *In thrombo-angiitis, however, when migrating phlebitis occurs, certain specific architectural changes can regularly be diagnosticated and found under the microscope.* An infectious agent is in all probability, responsible for the "acute" or earliest lesions. The evidences in favor of this view are discussed at length elsewhere.¹ It is of some interest to note that persistent leukocytosis has been observed in the early stages of this malady (Thomas²). In a case of extensive vascular occlusion of doubtful origin³ (obliterating thrombo-arteritis, possibly thrombo-angiitis obliterans) leukocytosis was present for a number of months. That something else must call forth or evoke such remarkable architectural complexes seems unquestionably true.

CHAPTER LVIII

THROMBO-ANGIITIS OBLITERANS—MIGRATING PHLEBITIS

There is no phenomenon of more importance in elucidating the true nature of the pathology of thrombo-angiitis obliterans than the characteristic thrombo-phlebitis or "migrating phlebitis" of this disease. The association of thrombosis of superficial veins of the upper and lower extremities with other evidences of obliteration of the larger arteries occurs in a sufficiently large number of cases to make the affection of the veins almost pathognomonic.

¹ Pathology of the Acute Stage, Chap. LXI.

² Thomas, Am. Jour. Med. Sc., 165, Jan., 1923, p. 86.

³ P. 474, Case G. G.

Those interested in a more intensive and comprehensive study of this disease will find a critical review of the clinical history of such cases of great value.

For the sake of clearness the cases of thrombo-angiitis obliterans attended with thrombo-phlebitis or migrating phlebitis may be divided into seven different groups. (1) Cases of thrombo-phlebitis without symptoms. (2) Thrombo-phlebitis with symptoms of limited vein involvement. (3) Migrating phlebitis causing the patient to seek treatment. (4) Cases in which both the migrating phlebitis and thrombo-angiitis obliterans play equally important rôles in the symptom-complex. (5) Migrating phlebitis involving both the upper and lower extremities. (6) Extensive migrating phlebitis of the chronic fulminating variety associated with a similar process in the deep and femoral veins; and (7) migrating phlebitis with a long prodromal phase, evidences of deep arterial involvement being lacking over an extended period of time.

I. THROMBO-PHLEBITIS WITHOUT SYMPTOMS

There are patients who have no knowledge of the occurrence of any trouble in the veins of the leg, but in whose amputated limbs extensive old, or old and recent thrombo-phlebitis of the internal saphenous or its tributaries is discovered. Such a case was J. C., who could recall nothing referable to a disturbance in the superficial veins. Study of the vessels revealed old occlusion of a large part of the saphena by virtue of a thrombotic process, and some areas of more recent thrombo-phlebitis. Sometimes an augmented streak corresponding to the course of the internal saphenous with induration under it, may be a definite evidence of a healed thrombotic lesion in the corresponding vein.

Case 1. J. C., 45 years, Russian Hebrew, admitted May 18, 1908; has eight children (all well); gives a rather typical history of vascular disease of both lower extremities, resulting in amputation of the left leg at the knee. Four years ago he had "rheumatism" of the right leg with pain in the sole of the foot and redness of the toes lasting eight months. Since then it has not troubled him. The left leg, however, began to hurt him last summer; he could not walk a block without taking a rest. His big toe became "sore" recently, and now the pain in the foot is constant. He is told that the big toe is becoming gangrenous, and that his leg should be amputated, which he gladly permits.

With the observation just cited, no new clinical facts are adduced, but certain similarities between the thrombotic lesions of the saphenous vein, as seen under the microscope, and the changes characteristic of the closed deep vessels were deemed sufficiently suggestive to warrant the suspicion that here, in the superficial veins, a new territory for the process "thrombo-angiitis obliterans" had been found.

II. THROMBO-PHLEBITIS WITH SYMPTOMS OF LIMITED VEIN INVOLVEMENT

A more interesting group is represented in those patients who come to us with active thrombo-phlebitis and periphlebitic manifestations. Here and there along the course of the internal or external saphenous vein, alterations in the skin and subcutaneous tissues occur. These are in the form of small, erythematous, slightly indurated patches, about a centimeter in diameter, and tender to the touch. Were it not for the concomitant phenomena referable to the tributaries of the saphenous or the trunk itself, the nature of these cutaneous nodosities would have remained obscure. With the appearance

of these, however, or at other times in the course of the disease, cord-like thickenings of portions of the long saphenous, with or without adhesion to the skin, are frequently observed. As examples let us briefly tell the story of Cases 2 and 3 in Group II.

Case 2. S. S., 30 years old, Russian Hebrew, admitted July 8, 1907; father of one child; has been suffering for four years with "weak legs;" for two years there has been pain in his left foot. About one and one-half years ago the second toe became gangrenous and was removed. Last winter his attention was directed to the blueness of the toes; it was difficult to keep the left foot warm. *For a couple of years he has noticed that "red spots" come and go along the inner and outer side of the shin bone.* They are a little painful and disappear without treatment. Now he seeks advice because the little toe looks as if it were going to die off. *Amputation* just above the middle of the leg.

Diagnosis.—A typical case of thrombo-angiitis obliterans with gangrene of the little toe of the left leg and cutaneous nodosities along the course of the internal saphenous vein from the ankle up to the region of the tubercle of the tibia; probably closure of a part of the saphenous vein.

The study of the vessels of the amputated leg showed extensive occlusion of the posterior tibial, anterior tibial, peroneal, and plantar arteries (thrombo-angiitis obliterans). The long saphenous vein was filled for the most part with old organized tissue of a type indistinguishable from that seen in the deep vessels, and some of its tributaries were closed by more recent obturating masses. The cutaneous nodules correspond to the distribution of the finer tributaries, but inasmuch as they had almost completely disappeared at the time of operation, no histological examinations were made.

As representative of the occurrence of migrating thrombo-phlebitis of the long saphenous and of erythematous nodosities in the same patient, let us cite Case 3, who observed and related quite accurately how the painful "hard cords" developed.

Case 3. F. S., 37 years old, Russian Hebrew, father of two healthy children, April 13, 1909; says that he remembers having had peculiar pains in the soles of both feet on walking a few blocks for the last three or four years. About four months ago the big toe began to trouble him, but even before that he noticed *hard cords* along the inner side of the leg. Since then the nail of the big toe came off, leaving a raw wound which refuses to heal. The long, hard strands come and go; sometimes they are seen high up on the leg; at others, three or four inches above the ankle. *Besides this there are lumps farther back on the inner side of the leg.* Patient does not return for treatment, so that the further course of the disease is unknown.

On physical examination the usual signs of thrombo-angiitis were found, with a trophic ulcer of the big toe. There were no evidences of recent thrombosis of the long saphenous other than one hard node four inches above the ankle; evidently the last attack of thrombo-phlebitis had subsided. The other leg showed somewhat less advanced symptoms of the disease.

Here, then, we are dealing with a case in which both the patient's narrative and ocular evidence point to the association of superficial and deep thromboses.

III. MIGRATING PHLEBITIS CAUSING THE PATIENT TO SEEK TREATMENT

When the attacks of migrating phlebitis make their appearance early in the history of the case, and when the attendant discomfort and pain are sufficiently great, then the symptoms belonging to the true, deep-rooted affection—*thrombo-angiitis obliterans*—are sometimes wholly ignored by the patient and remain undiscovered by the physician. Medical advice is sought only for the "lumps" and "hard, tender strands" or "cords" that are oftentimes so disturbing. Such observations are of no mean importance in diagnosis, since they have taught the author *to seek for the early subjective and objective signs of thrombo-angiitis in every patient in whom there are spontaneous and unaccountable attacks of inflammation of superficial veins.* Let us

see what we can learn, then, from Group III, in which migrating phlebitis causes the patient to seek treatment.

Case 4. E. B., 36 years old, Austrian Hebrew, consulted me on January 17, 1909, with the history of having had stinging sensations on the inner side of the right leg, low down, some three months previously. A few days after the onset of this trouble he could feel a long, thickened "*lump*" behind the shin bone, a short distance above the ankle. Soon after this, another swelling, not unlike a "*hard cord*," appeared somewhat higher up on the leg, was very tender, and was succeeded not many days later by a third somewhat shorter strand.

Upon close questioning he admitted that although he seeks relief from the symptoms mentioned, he has been annoyed for almost a month before the beginning of the present affection by frequent *cramp-like pains* in the calf of the right leg upon walking a few (five or six) blocks.

Physical examination, January 17, 1909, revealed induration of the tissues about the saphenous vein, from the ankle to the upper fourth of the leg. The distal portion presents a cord-like thickening, with scarcely any inflammatory signs. Higher up, however, the skin is adherent to the deeper hardened area, and is exceedingly tender to the touch.

The *dorsalis pedis* and *posterior tibial* arteries of both legs are *pulseless*; the femorals and popliteals can easily be felt to beat. The big toe of the right foot has a cyanotic hue.

Course.—January 31, his phlebitis was found much improved; his right big toe often hurts him, and his foot easily gets "cold" and "tired."

Two months later, March, 1909, no evidences of the old thrombo-phlebitis can be found. The big toe of the right foot still shows a peculiar bluish discoloration, and the absence of pulsation in the vessels is the same as before. *There are no trophic disorders*; the most striking phenomenon is the vasomotor disturbance in the big toe.

In short, we have here an exquisite example of a combination of early manifestations of thrombo-angiitis obliterans (pain on walking, evidences of disturbed circulation), with attacks of thrombo-phlebitis in the territory of one of the saphenous veins.

Whereas pathologic proof of the correctness of the diagnosis—thrombo-angiitis obliterans—is lacking in the last case, the history of another patient will be given in whom there were similar symptoms, and in whose amputated limb and excised veins ample material for anatomical investigation was found.

Case 5. M. K., 44 years, Russian Hebrew, father of three healthy children, was admitted to the hospital on December 8, 1908. His limbs never troubled him until about a year ago, when he felt the presence of tender spots on the inner side of the right foot. Soon other hard "lumps" and "cords" appeared, some of these in the neighborhood of the ankle, others higher up on the leg. After two months these disappeared, only to recur after a very short interval. Since then he has never been absolutely free from peculiar "painful spots," and now, on admission, he still has signs of some of them. About three months after the onset of these symptoms he experienced pain in the big toe, especially on walking. This has become gradually worse, so that he has been unable to get about properly for almost two months. Of late he has often had cramps in the calf and instep of the right leg after walking for a short distance. His chief complaint, however, is the painful condition of the inner side of his right leg.

Physical examination showed evidences of circulatory disturbance in the right lower extremity. Both the *dorsalis pedis* artery and the *posterior tibial* were pulseless, although pulsation of both the femoral and popliteal arteries could be easily detected.

Over the inner border of the right foot there is a red streak about one-half inch in length. This corresponds to a tender indurated mass which thins out and is lost as it is traced upward. A short distance below the middle of the leg the upper end of a hard cord can be palpated. This extends down behind the border of the tibia for more than two inches, is adherent to the skin, somewhat nodulated, and marks the center of an area of hypersensitive, swollen, turgid skin. There are no trophic disturbances. *Diagnosis—thrombo-angiitis, and thrombo-phlebitis of the internal saphenous and some of its tributaries.*

On December 15, 1908, a portion of the thrombosed saphenous was removed for pathological examination.

On December 26, 1908, the physical examination was recorded as follows: In the horizontal position the right foot has a light shade of red; this is most marked over the big toe, and fades off towards the ankle. In the web between the third and fourth toes there is a

superficial ulcer. On the inner side of the foot, almost two inches from the internal malleolus, there is a hard, cord-like nodule which is adherent to the skin. Behind the tibia there is a scar left after removal of a portion of the saphenous vein. The saphenous vein can no longer be felt.

On elevation of the foot, blanching sets in rapidly and pain becomes intense. The pendent foot turns very red (marked erythromelia).

Further Course.—February 15, 1909, the pain in the foot has been getting steadily worse, and the fourth toe is beginning to turn black. On the 23d of February amputation at the knee was done, at the request of the patient, for early gangrene of the fourth toe.

The prognostication that was made clinically in regard to the condition of the long saphenous vein was confirmed by pathological examination of the limb for, practically the whole of the main trunk of this vessel was found converted into a fibrous cord, the result of an old thrombotic lesion, similar to that found in the deep vessels. As for the arteries, the plantars, peroneal, posterior tibial, and lowermost portion of the popliteal were completely occluded by the brownish organized tissue usually encountered in the disease under consideration, whilst the deep veins were patent throughout.

Stated succinctly the case is one of thrombo-angiitis obliterans, in which the symptoms manifested themselves first in the form of migrating phlebitis that has persisted almost the whole of the years' course of the disease. The thrombotic lesion has affected the right leg and is associated with the development of typical symptoms of thrombo-angiitis. At the end of the year some of the deep vessels are closed, for there is absence of pulsation in the dorsalis pedis and posterior tibial. For a long time there are no trophic disturbances, but finally in the thirteenth and fourteenth months of the disease, ulcers develop and dry gangrene of one toe leads to amputation of the limb.

When the migrating phlebitis is a prodromal manifestation of the disease, thrombo-angiitis obliterans, or, if it marks a relapse in an apparently healed case, no phenomena referable to obliteration of the deep vessels may be obtainable. In such instances the excision of the affected superficial vein, followed by microscopic examination, will frequently reveal the typical pathognomonic lesions upon which a correct diagnosis may be based.

Case 6. H. P., 42 years, Russian Hebrew, seeks advice for a hard lump in back of the left leg on November 15, 1912. Twenty years ago the tip of the big toe of the right foot was removed in Russia, ostensibly for frost-bite. Since then (the exact date being unknown) the second toe of the same foot was also ablated. Save for these affections, no symptoms referable to the extremities can be recalled by the patient.

Physical examination shows a small thrombosed nodule, apparently associated with a varicose vein, over the calf of the left leg. In the vicinity there are small nodules, seemingly connected with tributaries of the external saphenous. There are no evidences of closure of the peripheral vessels.

Histological examination of the excised nodule, December 7, revealed the typical lesions of thrombo-angiitis obliterans.

Summary.—We have here, then, a case in which the history of the loss of two toes points to the existence of an old-standing thrombo-angiitis obliterans, the disease having become spontaneously cured. Recently there have developed evidences of involvement of superficial veins, the histological studies corroborating the diagnosis.

Another striking instance of the cases in which the thrombo-angiitis obliterans symptoms are masked and not noticed by the patient, and where the patient seeks advice because of migrating phlebitis, is presented by the following case:

Case 7. J. W., Russian Hebrew, consulted the author in November, 1911, because of red lumps in the left leg, and indefinite pains. He thinks he had syphilis 16 years ago, and that the lumps now present are due to this disease. The present trouble dates back about six weeks.

Physical examination shows a number of nodules of the usual type over the outer and posterior aspects of the left leg, and along the course of the internal saphenous vein.

On November 26, one of these nodules was removed for microscopic examination. Pathological examination shows the typical lesions of thrombo-angiitis obliterans in the early stages, typical giant cells, and miliary foci. Wassermann reaction on the 26th of November was negative.

December 4, some of the nodules had disappeared completely. The internal saphenous vein can be felt as a hard cord one-half way up the leg.

February 16, 1912, a fresh nodule has appeared above the Achilles tendon, another over the left calf, still another over the outer side of the leg above the external malleolus.

The dorsalis pedis and posterior tibial vessels of the right leg pulsate. The dorsalis pedis of the left does not pulsate. The posterior tibial pulsates very faintly.

We may cite as exemplifying cases of this group, the following history.

Case 8. B. C., 39 years, Russian Hebrew, seeks advice on account of pain in the left leg, which came on about four months ago. This seems to be associated with a nodule on the inner side of the middle of the tibia, and a similar nodule somewhat lower down. Three weeks ago another lump appeared on the outer aspect of the right leg. He has no pain on walking, and none of the symptoms of thrombo-angiitis obliterans.

Physical examination, December, 1911; several typical phlebitic nodules over the inner aspect of the left leg. The internal saphenous vein, from a point just above the ankle up to the upper fifth of the leg, can be felt as a hard cord. Anteriorly, three inches above the ankle there are two fused nodules in a somewhat reddened skin.

The dorsalis pedis and posterior tibial arteries are not felt in the left leg. The posterior tibial pulse of the right leg is also imperceptible, though the dorsalis pedis pulsates faintly. There is no erythromelia, but moderate ischemia on elevation of both limbs.

In short, we have here a case in which the symptoms of migrating phlebitis are prominent, the pulseless vessels and slight ischemia being the only evidences of thrombo-angiitis obliterans.

On December 5 one of the nodules was removed from the left leg for microscopic examination.

December 16. The phlebitis is extending from the region of the excised nodule in the upper part of the leg, and a distinctly tender cord, some $2\frac{1}{2}$ inches long can be felt along the course of the saphenous.

December 22. The nodules in the right leg have almost disappeared.

Still more interesting and instructive are those cases in which the disease of the superficial vessels affects both legs and one or both thighs.

IV. BOTH MIGRATING PHLEBITIS AND THROMBO-ANGIITIS PLAY EQUALLY IMPORTANT RÔLES IN THE SYMPTOM-COMPLEX

The following case will illustrate this variety. The patient could be observed for almost a year, the progression of the obstructive changes in the deep vessels could be closely followed by proper interpretation of the varying circulatory phenomena in the leg, and many of the attacks of thrombo-phlebitis in the territory of at least one saphenous vein could be recorded.

Case 9. H. R., 32 years, Russian Hebrew, August 9, 1908, has been suffering for five years. At first it was a burning sensation in the toes of the left foot that gave him most concern, but later on he was troubled more by his inability to walk distances on account of the sudden advent of attacks of pain that were felt from the toes upward almost to the knee. In cold weather he seems to be in poorest condition, for then his toes get cold and blue, and walking is very difficult. Although this has been going on for years, he has not found it necessary to consult a physician until something else in his *right leg* began to engage his attention.

For the last five months long "streaks" or "swollen places" would come and go over the inner side of the right leg, behind the shin bone. These are often very painful. A week ago a physician told him that he had "phlebitis."

Physical examination on August 17, 1908. The vessels of the right leg pulsate, but the left posterior tibial and dorsalis pedis cannot be felt.

The right leg shows a tender cord with some edema around it, extending from the ankle almost to the tibial tubercle. This corresponds to the long saphenous. Erythromelia is

definite on the left side, there are no trophic disturbances, and the circulation of the right leg is fairly good.

From now on aggravation of his subjective condition went hand in hand with the advancing lesions in the vessels. That an increase in the extent of vascular occlusion took place from this time on could be easily deduced from clinical observation.

On December 1, 1908, the following was recorded: The right foot looks pale (evidence of the beginning of circulatory disturbances). After a short time it becomes slightly cyanotic. It looks cadaveric when raised for a short time. There is no erythromelia. The dorsalis pedis does not pulsate. A tributary of the long saphenous about two inches long can be palpated as a tender cord along the lower inner aspect of the right thigh; the skin over it is reddened. There are two nodosities in and under the skin below and to the inner side of the tubercle of the tibia. The left leg shows marked erythromelia; blanching in the elevated position is extreme; the popliteal is open, but the dorsalis pedis and posterior tibial arteries cannot be felt. There are no ulcers or other signs of trophic disorder.

The steady advance of the occlusive process in the deep vessels is well illustrated by the findings on December 1, 1908. In August all the vessels of the right lower extremity pulsated in normal fashion; now, in December, the dorsalis pedis is occluded. Corresponding with this there is a new symptom, the blanching of the foot. How remarkable that the disease of the deep vessels on the right side should be so closely associated with the attack of migrating phlebitis, the latter first attacking the saphenous in the leg, and now appearing in the thigh! We have evidences of chronicity in the affection of the superficial veins, and as regards the deep lesion, we have been able to watch its gradual development both by its effect on the palpable arteries and by the clinical manifestations it has produced.

On January 31 the big toe of the left foot was swollen and red; the nail was coming off. Immediately upon removing his shoe, the right foot had a very white color, but soon cyanotic patches mingled with the pallor all over the foot, especially in the region of the big toe. The pain in the left foot was now excruciating and he consented to an amputation with scarcely any reluctance. The left leg was amputated at the upper fourth.

Examination of the vessels of the amputated limb showed occlusion of the following arteries: Dorsalis pedis, peroneal, plantars, and posterior tibial. The anterior tibial artery was open throughout most of its course. A large part of the long saphenous vein was found occluded by an organizing thrombotic process.

Diagnosis.—Thrombo-angiitis obliterans.

In short, this patient presents the following features of interest: (1) Migrating thrombo-phlebitis of both saphenous veins; (2) involvement of the same vein in its course through the thigh; (3) associated progressive and synchronous development of the thrombosis in the *superficial* and *deep* vessels of the right lower extremity; and (4) absence of any cause for the lesion of the superficial vessels.

Case II. W. T., 26 years, Russian Hebrew, admitted July 10, 1909.

In April, 1907, he was treated for gangrene of the third toe of the left foot. Three months before admission to the hospital he had been suffering with pain in the left calf and foot. During the previous winter (1906) the left foot did not seem to be normal, so that he sought the advice of an orthopedist, who gave him the usual treatment for flat feet. Later, he has had severe pain in the calf, and shortly before admission gangrene of the third toe set in. He had an amputation performed on the 27th of May, 1907, the left leg having been ablated at its upper third.

At that time pathological studies revealed the usual changes that are seen with thrombo-angiitis obliterans: The dorsalis pedis, posterior tibial, the greater portion of the peroneal and plantar arteries were closed.

Present Status (1909).—Since discharge, June 27, 1907, until eight months ago, he seemed to be doing well. About this time (8 months ago) he noticed the appearance of red streaks and nodules on the inner side of the right thigh. After a few days these would disappear and new ones would appear in their stead, either higher up on the thigh, or near the knee. They caused a peculiar pricking sensation, and some were tender and painful. Lately, he has been able to walk no more than two hundred steps without resting.

The external manifestations on the 10th of July, 1909, were as follows:

A healed amputation scar in the left leg. In the dependent position there is marked erythromelia of the right leg. Neither the dorsalis pedis nor the posterior tibial can be felt to pulsate. On the inner side of the thigh, near its middle, there is a sensitive strand, which corresponds to the thrombosed saphenous vein. On the outer side there are a number of hard, indurated, reddened nodules. Over the inner side of the dorsum of the foot there are similar nodules and strands.

Diagnosis.—Migrating phlebitis and thrombo-angiitis obliterans.

In short, the history of this case reveals the following: Thrombo-angiitis obliterans first involving the left lower extremity, leading to amputation; insidious development of the same disease in the right lower extremity, with extensive thrombosis of the superficial veins of the thigh and leg.

From the consideration of the data thus far presented it would appear that the internal saphenous vein is the site of predilection for that peculiar lesion which is termed a migrating phlebitis. In July, 1904, the author had the opportunity of studying a case in which the veins of the upper extremity, too, were involved. Since then several additional patients with a similar distribution of the lesions have come under observation.

V. MIGRATING PHLEBITIS OR THROMBO-PHLEBITIS INVOLVING BOTH UPPER AND LOWER EXTREMITIES

In three out of four of these patients the disease has reached that stage of chronicity in which the suffering is almost constant and in which the limbs may be regarded as irretrievably lost. For there are cases that become "cured" as far as symptoms are concerned. And by "*cured*" in this sense we do not mean to imply that the pulseless dorsalis pedis, posterior tibial, or both, begin to beat again, but rather that, in spite of closed vessels, an adequate collateral circulation has become established, as evidenced both by the absence of the typical manifestations of impaired circulation, and by the patient's improved subjective state. These three patients *per contra* had the "severe" form of the disease, even though the issue, gangrene, was delayed far beyond our expectations.

Case II. B. B., 34 years, Russian Hebrew, married, has no children; operator for eleven years. His malady began eight years ago, when he first experienced pain in the right calf on walking. He would be compelled to rest after walking four or five blocks. At about the same time he often noticed that there were long "hard cords" and "reddened lumps" over the front of *both forearms* (anteriorly) and over *both legs*. These would come and go, appear with provocation, now in an arm, now in a leg. The lumps were always small, pea-sized or slightly larger, and could be felt for two or three days.

He always felt better during the summer months. The nodules in the legs were present almost every winter for the first five years. Six years ago there was a "bad attack," in the course of which there were ("Adern") "veins" or "nodules" behind and above the right ankle. Then again, about three years ago, there was a repetition of this trouble. Nodosities formed behind the shin bone on the inner side of the right leg (region of saphenous) and the pain kept him abed for almost ten weeks.

Thus, up to this time he complained of the following: Pain in the right calf on walking two to four blocks, painful nodules and cords, and cramps in the toes and sole of the right foot at night.

For two years the left leg has given him concern; the condition is practically the same as that of the right. Last winter, January, 1909, there were "sores"—one at the tip of the big toe of the left leg, and another at the end of the little toe of the right. He feels best when his legs hang down (a variation from the usual statement); but even in this position the toes often feel "dead." In the same way his fingers get "numb" in winter; he thinks that there is no blood in them.

Physical Examination.—In the right leg the toes have a tense, reddened appearance, the second and third being discolored most, the little toe having a cyanotic hue. Just behind

the nail on the plantar surface there is a deep fissure, the tips of which are adherent. Slight pressure brings forth a drop of pus from the bottom of the wound. The erythromelia is marked over the dorsum of the foot, as well as over the sole. Ischemia in the elevated position is intense; this posture excites severe pain. The femoral artery pulsates; the popliteal, posterior tibial, and dorsalis pedis cannot be felt.

The left leg is similarly affected; the rubor is deeper and the toes are more swollen. There is a trophic ulcer at the tip of the big toe. The ischemia, too, is of a greater degree. All the vessels (femoral included) fail to pulsate.

Summary.—This is a case which, according to the story, combines thrombo-angiitis obliterans with migrating phlebitis of both upper and lower extremities.

One of the most instructive cases of this series is a patient in whom the attacks of inflammation and thrombosis of superficial veins *dominated* the clinical course *for years before the symptoms characteristic of thrombo-angiitis obliterans came into evidence.*

Case 12. D. B., 35 years, Russian Hebrew, first seen by the author July 16, 1904. He had been treated in the hospital eight years previously for "phlebitis" of the right leg; a portion (5 inches) of a large vein was diseased at that time, and the history states that the process was "migrating," moving up and down the thigh. He says that this trouble lasted off and on for two years. In 1903 there were "lumps" in and under the skin of the right leg, and then, three months later, in the left leg. Such swellings would last a week, develop into hard "tender spots" with a covering of red skin, and on one occasion three such spots appeared on the left arm, in front of and just below the elbow.

Physical examination, July, 1904. In the left antecubital region there is a thickened, slightly reddened cord about two inches long. Another is situated on the ulnar aspect of the same forearm, near the elbow. The right forearm presents a similar vein about three inches from the elbow; the skin is not reddened. On the inner side of the right cubital space a subcutaneous adherent nodule can be felt; it is very tender. There are several such nodules in the right calf and smaller ones over the left shin bone. No edema, but slight cyanosis of both legs in the pendent position. A portion of one of the thrombosed arm veins was extirpated for study.

Course.—A year later, 1905, symptoms referable to affection of the deep vessels of the left lower extremity manifested themselves, to wit: Coldness and blueness of the left foot and superficial ulcers on the toes.

Thus far our patient presented no striking addition to the symptom-complex under discussion, other than the thrombo-phlebitis of the arm veins. In 1907, however, he developed a gangrenous patch at the tip of the middle finger of the right hand. This rather unique site for trophic manifestations is rarely seen in obliterating thrombo-angiitis, and therefore deserves more detailed mention.

February 1, 1907, D. B. stated that his doctor had been treating him for a "felon" of the middle finger of the right hand. His hand had been cold for several weeks, and the middle finger was painful. Four weeks previously a black "dead" spot formed on the tip of the finger, and since then, what with cutting it and self-treatment, he thought that the present intensely painful affection had overtaken him.

Physical examination, February 1, 1907. A portion of the tip of the middle finger is gangrenous; there is no infection; the distal phalanx seems to take part in the process of mortification. On the dorsum of the hand, just over one of the veins, there is a bean-sized indurated area; the skin over it is adherent and tender. About one inch above the wrist, behind the radius, there is a reddened hard cord, more than an inch in length (doubtless a thrombosed vein).

The left foot is bluish, and there are a number of red nodosities in the leg. They are placed over the course of the long saphenous vein, one or two inches above the tip of the malleolus, and a couple of others three to four inches above the ankle. The right leg shows a thrombo-phlebitic, indurated process over the lower part of the anterior tibial group of muscles.

Further Course.—The finger improves very slowly; in April it is healed. The nodules in the upper extremities disappear after three weeks. April 16, 1907, over the outer side of the right leg, four inches below the tibial tubercle, the skin and subcutaneous tissues are indurated. There are two hard areas farther down. The nodosities come and go, now in the right and now in the left leg. On April 29, 1907, his left foot troubles him greatly. It is slightly swollen; the toes become deep red in the dependent position. The right foot is slightly red in the same position. The femorals and popliteals pulsate well. On June 1 the left foot is very painful; the toes feel as if needles were sticking them.

November, 1907. Since the beginning of September the right leg seems to be affected by the same disease as the left. New nodules of subcutaneous infiltration have appeared on the inner side of the left leg and the inner side of the right knee. They seem to have very little tendency to disappear. He often has pain in the middle finger of the right hand, and this hand is colder than the left.

Physical Examination.—On holding both hands above his head the right becomes blanched. When the hands hang, the right becomes cyanosed; there is an admixture of red, so that there is a mottling of red and blue (erythromelia of the upper extremity). Both radial pulses are good. *Lower Extremities.*—On the inner aspect of the right leg three nodules are seen, two near the tubercle of the tibia, a third one inch behind the middle of the crest of the tibia. They are $\frac{3}{4}$ to 1 inch in diameter, involve skin and subcutaneous tissues, and are red. Similar infiltrations are found on the inner side of the left leg, two in the middle and upper third; two others four inches above the ankle. They evidently follow the course of the saphenous vein. The right foot has a bluish red color. The left is even more markedly discolored; the second toe is enlarged, looks angry, and presents a small superficial ulcer near the nail. On December 19 (a warm day) the legs are red when they hang down. There is no cyanosis. Both feet become cadaveric when raised. A new cord has formed over the right wrist; it is about an inch long, and lies over the radius; a somewhat longer cord is situated over the inner side of the right knee. (Mercury injections are administered.) January 3, 1908, the dorsalis pedis and posterior tibial arteries are pulseless. February 7 he still has the painful cord over the right wrist, although he has had seven injections of mercury. The right popliteal pulsates, the left pulsates faintly; both femorals are open.

September 7, his right foot is worse than the left. The dorsalis pedis and posterior tibials of both legs are evidently closed. At this time the right popliteal does not pulsate; the left beats faintly (note that this corresponds with the aggravated subjective sensations of the leg); both femorals are felt. Recent ulceration has occurred in the web between big and second toes of the right foot. The toes are intensely red in the dependent position. On November 19, in the horizontal position both feet possess a marked erythematous hue.

On April 13, 1909, the patient came to the hospital for the ulcerated condition of both feet; he cannot walk. Over the dorsum of both feet there are superficial ulcerations, and there are a number of trophic ulcers in the webs of several of the toes. Under rest in bed and local treatment all the wounds heal. By June 9 both legs are in a condition of chronic erythromelia, even in the horizontal position. The feet have a dusky red hue; in the dependent position there is an admixture of purple. The skin is shiny and appears thinned, although the toes themselves are enlarged. Only the femoral arteries pulsate; the ischemia in the elevated position is very marked; all the superficial ulcers have healed.

Summary.—The total history up to the present time extends through a period of about twelve years. During the first eight years the clinical course was characterized by repeated attacks of migrating phlebitis of the superficial veins of the upper and lower extremities, and the appearance of cutaneous nodosities, due in all probability to circumscribed venous thromboses. These attacks were accompanied by the usual pain and tenderness, some edema and secondary cutaneous manifestations. Towards the end of the first period the prodromal indefinite pains of typical thrombo-angiitis were noticed. These were followed by the development of marked erythromelia of the left lower extremity, and of trophic disturbance. Then came a cessation of the process on that side, only to give way to a similar diseased condition on the right side, where it has caused obliteration of the distal vessels and the popliteal. In short, a period of occlusion of superficial veins was followed by a period of arterial occlusion which attacked first the left, and then the right leg.

Does the paroxysmal nature of the involvement of the superficial veins throw any light on the sequence of events in the deep vessels? From previous pathological studies¹ it seemed most plausible to assume *that certain territories of either arteries or veins become rather suddenly thrombosed*, in a fashion similar to the superficial venous thromboses of the lower extremities. The history of the thirteenth case is exceedingly illuminating on this point, since it suggests that attacks of migrating phlebitis of one leg may occur

¹ Am. Jour. Med. Sci., October, 1908.

synchronously with paroxysmal pains in the other leg, and that these latter pains are closely associated with other signs clearly pointing to an exacerbation of the thrombotic lesion in the deep vessels—"an attack (if we may so regard it) of *thrombo-angiitis obliterans*." In other words, it seems more than likely that, at any given time, *the patient may be suffering from a more or less acute disturbance, in the course of which both superficial and deep vessels become closed.*

Case 13. M. P., 34 years, Russian Hebrew, admitted to Mt. Sinai Hospital in May, 1908. My history was taken on May 24, 1908. Two years ago there were some "swollen places" on both legs, and he had pain in the legs when he walked. One year ago he had attacks of "phlebitis;" this was the diagnosis at the Presbyterian Hospital. The veins on the inner side of the left forearm and arm, almost up to the armpit, were painful. The left saphenous at the middle of the leg was also diseased at that time. He had been treated at Mt. Sinai Hospital in August, 1907, for "phlebitis migrans." At that time no suspicion was entertained as to the existence of the condition, thrombo-angiitis obliterans.

Last winter he often had pain in the feet on walking, and this has been much worse for the past four weeks. During the last two months the symptoms of phlebitis have recurred in the left leg and the left arm.

Present History.—For four days he has had excruciating pains in the calf of the right leg, even when in bed. Besides this, he has painful cords and "spots" in his left leg.

Physical Examination.—Both radials pulsate. The patient seems to be very restless because of the pain in his right leg. In the right leg neither the dorsalis pedis nor the posterior tibial artery can be felt; the popliteal artery is patent. The toes are slightly red in the horizontal position; there is marked erythema of the toes in the pendent position. Ulcers and thromboses are absent. (Note made May 24: The pain in this leg must be interpreted as suggesting thrombosis of the deep vessels, because there is nothing else to account for his suffering; apparently no neuritis.)

In the left leg also, absence of pulsation in the dorsalis pedis artery and posterior tibial artery is noted. Just behind the tibia, at the middle of the leg, the saphenous vein is thrombosed, being adherent to the skin, which is reddened. There are a number of nodules in its vicinity, probably corresponding to small tributaries. There is erythromelia of moderate degree, but no marked ischemia in the elevated posture. The popliteal artery is patent.

In the left arm a small portion of an anterior ulnar vein, low down, is indurated.

Briefly, then, the typical signs of bilateral thrombo-angiitis obliterans, without trophic disturbances, varicose veins, or infection, are associated with attacks of thrombo-phlebitis of the superficial veins of the upper and lower extremities.

On May 28, 1908, the pain in the right leg is gone, the cords are disappearing, the ulnar thrombosis is no longer palpable.

The patient again seen on December 1, 1908. After leaving the hospital he could walk but a block without stopping for a rest. For about two weeks a new longer cord has traveled up from the middle of the inner side of the left leg, behind the knee, to the lower part of the thigh. There is another one behind the ankle and inner side of the foot. In the calf there are two tender bean-sized nodosities. He says that the big toes always feel as if they were asleep, and he often has an inclination to rub them to dissipate the feeling of numbness. Examination shows his condition to be slightly worse than it was in May, as regards sufficiency of circulation in both legs.

On June 15, 1909, he was again examined, then a pitiful spectacle to behold.

Pulling himself along on two crutches, with an expression of fear written all over his face lest the contact of the soles of his feet against the ground call forth excruciating pain, with the aid of his wife he finally seats himself, telling me the following story: He has tried "everything" for his legs. He has been treated in other hospitals since I last saw him, and now he cannot walk at all. The big toe of the left foot hurts him unbearably, and his physicians are unable to ward off the coming of those dreadfully painful "sores" and "fissures" that form without reason on his soles, between the toes, and near the borders of the nails. He cannot bear his weight on the legs at all. The effort to walk was soon given up and he has permanently assumed the horizontal position as the only one possible to be borne.

Physical examination shows intense erythromelia of both feet, with a slight cyanotic hue, as in Case 12, D. B. The middle portion of the internal saphenous vein for about an inch of its course through the leg is converted into a hard, tender cord. There is a nodosity 0.5×1 cm. three inches below the left tibial tubercle and two inches outside of the crest of the tibia. All the toes of both feet are somewhat enlarged; they look stiff and turgid when held in the dependent position. The blanching of the raised feet is extreme.

Résumé of Case 13.—Recurring thrombo-phlebitis migrans of both upper and lower extremities, gradual development of the severe chronic clinical type of thrombo-angiitis obliterans without gangrene, symptoms indicating the simultaneous paroxysmal attack of superficial and deep vascular channels.

One of the best examples of extensive disease of the veins in all four extremities is that presented by Case 14. Because of the development of an adequate collateral circulation, obstruction and closure of the deep vessels had apparently produced no symptoms in the left leg, whilst the disease had made considerable progress in the right leg. Signs of an active migrating phlebitis could be found only in the lower extremities, but the definite statements of the patient leave no doubt as to the correctness of the view that he had had attacks of phlebitis in the upper extremities at one time.

Case 14. M. G., 37 years, Russian Hebrew, married, has two healthy children, consulted me, August 6, 1909. Four years ago he had tender "cords" or "lumps" on both forearms and also on the inner side of the arms. These soon disappeared and have not recurred; at that time, however, there was also a similar condition in the calf of the right leg and inner side of the left leg. He was quite free from trouble until a year ago, when these painful spots also developed in the legs.

For three months he has had wakeful nights because of pain in both feet, especially in the right. His toes get cold and he cannot walk because of the sudden advent of cramps in the calves. The "cords" in the right leg have now disappeared, but they are still present in the left leg, where they come and go.

Physical examination, August 6, 1909. Both lower extremities present the typical signs of thrombo-angiitis obliterans. Evidences of circulatory insufficiency are most marked in the right leg, where there is distinct erythema in the horizontal and pendent positions. Both legs become intensely blanched when elevated. All three vessels (dorsalis pedis, posterior tibial, and popliteal) are pulseless on the right, whereas a very faint pulsation in the upper part of the left popliteal can be detected, the distal vessels evidently being closed. There are no ulcers.

Just below the middle of the course of the left saphenous a hard, knobbed, tender cord can be easily felt. At the inner border of the foot there is an erythematous nodule which is tender.

On August 8, about 1 inch of the thrombosed saphenous of the left leg was excised under local anesthesia for diagnostic purposes. The vein was filled with recent clot, and was fairly adherent to its bed, showing an active periphlebitis.

In September, 1909, the right leg was amputated three inches below the knee, because of gangrene of the toes.

On October 27, 1910, he says that there was considerable pain in the sole of the left foot, and that he could not walk more than two blocks without stopping for rest. Ever since the operation he has had recurrent attacks during which the same hard cords or nodules which he had before, developed in the left leg. Several of these have now been present for three weeks.

Physical examination, October 27, 1910, shows a nodosity in the middle of the left leg, and two or three confluent nodosities above the malleolus. There is marked erythromelia, and the pulses are absent in the popliteal, posterior tibial, and dorsalis pedis.

November 10, 1911. The phlebitic process is still present. Fresh nodules are making their appearance. The evidences of obliteration of deep vessels of the left leg are more striking, and the disease, thrombo-angiitis obliterans, is evidently making progress with signs of the development of trophic disorders.

Epicrisis. We are dealing here with a case of bilateral thrombo-angiitis obliterans with associated migrating phlebitis which had originally affected both forearms, and for more than two years has shown itself also in the lower extremity. The persistence of the migrating phlebitis, the chronicity of the deep vessels, and thrombo-angiitis obliterans of the left leg, are features worthy of note.

Here we are dealing with a case presenting active signs of thrombo-angiitis of the vessels of the lower extremities for three months. At the same time, there were recurring attacks of phlebitis of the upper and lower extremities. At times he sought advice because of the phlebitis; at other times, because of the symptoms referable to the deep seated disease. Four years after the onset of the disease the findings were as follows:

The results of advanced closure of the arteries of both lower extremities; absence of any recent or active symptoms in one of the legs; distinct signs of a slowly progressing involvement of the circulation of the other limb, with recurring attacks of phlebitis of the saphenous vein, without ulcers, trophic disturbances, varicosities, or evidences of inflammation.

VI. EXTENSIVE FULMINATING MIGRATING PHLEBITIS

By this type we mean cases in which from the very first onset of the thrombo-phlebitic process, there is not a single period of remission but attacks of migrating phlebitis follow in quick succession one after the other, so that the whole of the foot and the greater part of the leg and even the thigh are beset with the inflamed and indurated cords. That the process is a severe one and may have analogy in the deep veins was demonstrated by the clinical course and pathological findings in one of the cases (H. H.) in which at the time of amputation the popliteal vein was found in a condition of diffuse phlebitis and obturation with red clot, the femoral vein found to be likewise involved at a secondary operation.

Case 15. H. H., Russian, 36 years of age, consulted me on the 15th of April, 1916, with all the usual symptoms of thrombo-angiitis obliterans of both lower extremities, with absent dorsalis pedis, posterior tibial and popliteal pulsation on both sides, without migrating phlebitis.

From August 20, 1919 (probably several months before this, according to the history), until amputation was done on the 15th of March, 1921, a period of about two years, there had been a succession of attacks of migrating phlebitis, particularly over the left leg and thigh, which were exceedingly painful, and caused the patient to stay most of this time in bed.

On the 20th of August, 1919, there were evidences of thrombo-phlebitis over the internal saphenous of the left leg, that had, according to the history, been present for several months. On the 4th of November, 1919, the phlebitis had somewhat subsided, having lasted now about one-half year. In December, 1919, another attack of phlebitis took place.

On April 2, 1920, he said that for the last three months there had been constant attacks of migrating phlebitis with tender and red areas, making it impossible for him to work, and the right hand as well as both feet are cold at all times. Throughout the rest of the year attacks followed in quick succession so that the greater part of all the superficial veins were involved.

The pain in this case (as well as in others of this type) was excruciating by reason of the multiplicity of veins involved, and with this the limb seems to become daily more and more atrophic.

Finally, on the 15th of March, 1921, a Gritti-Stokes operation was performed, and not only was the popliteal artery closed by old organized clot, but the popliteal vein was occupied by a recent clot similar to that found in the superficial veins.

Contrary to the rule, this case *did not do well* after the Gritti-Stokes operation (being the only case in a series of more than sixty), since the peripheral portions of the flaps became gangrenous, the sloughing process continuing in spite of rigid asepsis and great care.

It became necessary, therefore, on the 26th of April, 1921, to do an amputation through the thigh, where an explanation for the inadequate circulation was to be found in the condition of a femoral vein, which was also closed by red thrombus.

Summary.—Extensive migrating phlebitis of two years' duration, with practically no remissions, a thrombotic process involving the femoral and popliteal veins, interfering with circulation to such an extent as to prevent healing, when Gritti amputation was done.

VII. CASES IN WHICH ABSOLUTE EVIDENCES OF DEEP ARTERIAL INVOLVEMENT ARE LACKING

Although our experience justifies the conclusion that the affection of the deep arteries or veins regularly follows the premonitory migrating phlebitis, even though years elapse, occasionally cases are observed in which evidence of arterial involvement is absent for so long a time that we are in some doubt as to the correctness of our diagnosis. Eventually at least one or more pulses become imperceptible even though local symptoms are lacking.

We may summarize briefly the history of one instance, in which the attacks of thrombo-phlebitis must have been distributed over a period of 8 years,

during which time signs of blockage in the deep vessels were not demonstrable. Finally, 10 years after the first attack of phlebitis, the posterior tibial pulses could not be felt.

Case 16. B. S., male, Russian, aged 36, gives a history of swelling and reddening of both legs of 8 years' duration, accompanied by "hardening" of the veins and inability to walk. Similar disturbances have been intermittently present in both upper extremities for the last 2 years.

Physical examination, August 23, 1920, none of the subjective or objective manifestations of thrombo-angiitis obliterans could be elicited in the lower extremities. There was a long cord over the ulnar half of the anticubital aspect of the forearm, and several tributaries of the external and internal saphenous of the right leg were the site of migrating phlebitis. A small vein of the right forearm was also involved. All the arteries of the lower extremities pulsate at the usual sites.

August 24, 1920, excision of a tributary of the left ulnar vein for microscopic examination revealed an occluded vein with thickened walls, and adherent to the skin, and its lumen filled with clot in very early state of organization. Microscopic examination revealed the typical picture of thrombo-angiitis obliterans in the *acute stage*.

December 1, 1922. There have been no symptoms since August, 1920; no intermittent claudication, no manifestations of impaired circulation of the lower extremities, and no recurrence of the phlebitis. Nevertheless, examination shows that *both posterior tibial pulsations have disappeared!*

These facts lead us to the following conclusions:

First, that the phlebitis plays no subsidiary rôle in the symptom-complex of some of these cases.

Second, that the disease, when it affects the upper extremities, is less enduring than in the lower extremities.

Third, that we have here another link in the chain of evidence speaking for an identical cause for the disease of the deep arteries and veins and the superficial veins.

CONCLUSIONS FROM VEIN LESIONS

In 1908 the author's studies of the pathology of nineteen amputated limbs in thrombo-angiitis obliterans had clearly demonstrated the thrombotic nature of the vascular occlusion. It was also shown that the pictures formerly interpreted as results of a thickening of the intima were produced by organization and canalization of red obturating thrombi. It was found that the disease involves the deep arteries and veins of both the lower and upper extremities, commencing by preference in the vessels of the foot, such as the dorsalis pedis and plantars and their larger branches, ascending so as to sometimes close even the iliacs and aorta. *Clinical and pathological data led to the assumption that the progression of the thrombotic process takes place rather in attacks or sudden exacerbations than by a gradual ascent; that larger or smaller territories of the deep vessels become suddenly closed, just as the saphenous veins are wont to be thrombosed and inflamed from other causes—in other words, that the process is a migrating thrombosis of the deep vessels comparable to the migrating phlebitis of the extremities.*

A cursory study would lead one astray as to the significance of the most common lesions seen in the arteries and veins, for it would fail to reveal the fact that there are *two distinct phases* in the pathology of the disease. The lesion most commonly encountered is but the result of the organization of thrombi, and of importance only in so far as it is productive of the pictures that may be confused with endarteritis obliterans. More interesting and more valuable for investigation is the "acute stage," or earliest lesion, that occurs simultaneously with, or shortly after the onset of the thrombosis.

This early stage was found by the author in the deep vessels of but two of the amputated limbs. In these certain specific morphological alterations were encountered, whose meaning was not understood at that time. These histological changes appeared to be characteristic of the disease, thrombo-angiitis obliterans, not having been met with in vessels thrombosed through other causes. The regularity of the occurrence of the typical lesions aroused the suspicion that here was a specific morphological alteration, due to a specific cause.

In short, whereas the usual changes in most of the vessels of an amputated limb represent the healed stage of the disease, that in which a fibrous mass containing canalizing vessels has taken the place of the original clot, there is another *early or acute stage* of the disease which alone is of value in throwing light upon the true nature of the process. It is only at this particular period in the history of the pathological process that the media is diffusely infiltrated with leukocytes, and that the lumen is filled with red clot, in which certain typical miliary giant-cell foci¹ make their appearance. It is these foci that lend a characteristic appearance to the thrombotic lesion of thrombo-angiitis obliterans.

When these lesions were first referred to in 1908 their significance was not understood, although the suspicion was already aroused at that time that they were specific for the disease and probably represented a peculiar reaction on the part of the tissues to some toxin or organism. It seemed clear, too, that it would be a difficult matter to obtain an adequate amount of material from the deep vessels for the study of the acute stage of the disease. It was here that we had to pause in our deductions, when we were fortunate enough to encounter a most interesting fact, that the superficial or subcutaneous veins of the upper and lower extremities may also be affected by the disease, thrombo-angiitis obliterans. Thus, in 1909, the association of migrating phlebitis of the subcutaneous veins of the extremities was noted in eleven cases. From a study of the clinical history of the cases, and of the histology of the affected subcutaneous veins exsected during various stages of the disease, the following conclusions were drawn:

1. The disease thrombo-angiitis obliterans is often associated with thrombo-phlebitis of superficial veins of the arms and legs.
2. Certain peculiar cutaneous nodosities are characteristic manifestations in many cases.
3. The disease of the superficial veins may be subsidiary or it may dominate the clinical picture. Objective signs referable to these vessels should be regarded as extremely suspicious marks of the synchronous development of thrombo-angiitis obliterans, in the form of pulseless vessels, erythromelia, blanching of the leg in elevated posture, cold and blue toes, pain in the calf of the leg brought on by walking, and other typical phenomena.
4. Migrating thrombo-phlebitis may give no symptoms, the signs referable to the deep vessels being of most importance.
5. Patients may suffer at one time from migrating thrombo-phlebitis, at another from the progress of the occlusive change in the deeper vessels.
6. Certain cases suggest the possibility that attacks of trouble in surface veins may occur simultaneously with similar exacerbations of disease in deep vessels of another limb.

¹ Buerger, *Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie*, 21 Band, 1919; also *Am. Jour. Med. Sci.*, October, 1908; and *Surg., Gyn. & Obst.*, Nov., 1914.

7. The morbid process resulting in the production of cutaneous nodosities and thrombosed superficial veins is independent of varicosities, of infection, or of trophic disorders in the territory which they drain.

8. The vessels of the upper extremity may be affected by the lesion thrombo-angiitis obliterans.

9. Thrombo-phlebitis in the arm and forearm should arouse suspicion as regards involvement of the deep vessels of the legs.

10. Further studies should be directed towards solving the relationship between the two thrombotic lesions. Perhaps excision of nodules and veins early in the disease, exploratory incision for inquiry into the condition of the deep vessels, and bacteriological and serum investigations along the proper lines will do much to enlighten us in our interpretation of this most puzzling symptom-complex. Although absolute proof is lacking, it seems more than probable that the same determining causative factor is responsible for the lesions of both the superficial and deep vessels.

Up to the year 1922 it was possible to gather data on additional cases in which the superficial veins were involved which increased the number of exsected veins up to thirty-five. In these, both the acute and healed stages of the disease were found. From a consideration of the pathological pictures the conclusion was reached that the specific characteristic lesion of thrombo-angiitis obliterans may affect the *deep as well as the superficial vessels*; that it is in the veins that we shall have to look to find material for investigation of the causative agent; and that not only do the superficial veins present the typical miliary giant-cell foci, but they also demonstrate that these foci are a later stage, or attempt at organization of purulent foci. In other words, the finding of miliary pus foci in the subcutaneous veins as precursors of the typical giant-cell foci was noted in a sufficient number of instances to warrant the conclusion that this lesion represents the acute stage of the disease, and suggested, too, that the thrombotic process may be caused by the presence of some organism, virus, or specific toxin.

CHAPTER LIX

THROMBO-ANGIITIS OBLITERANS—INVOLVEMENT OF THE UPPER EXTREMITIES

In about 500 cases of thrombo-angiitis obliterans observed from 1909 to 1922, the author was able to watch the course of this remarkable disease through all its clinical stages. Many of the cases were followed from five to fourteen years, and the presence of interesting mutations in the symptomatology could be recorded. It was found that in a certain number of the patients the upper extremities are involved, although it is usually believed that only the lower extremities are affected.

Early Symptoms of Involvement of the Upper Extremities.—Coldness and a feeling of numbness and deadness of the fingers may be the first symptoms in one or both hands simultaneously, trophic disturbances soon following. Patients describe these as being sores at the tips of the fingers that are exceedingly painful, that are sometimes followed by suppuration gradually healing, leaving retracted scars near the nail at the tips of the affected fingers. Pallor

of one or more fingers in cold weather is also mentioned by patients as a striking symptom.

Objectively, when seen several months after the onset of the symptoms, the picture of early involvement without gangrene and without trophic lesions is the following. The hands may show rubor and this is associated with coldness of the tips of the fingers. This combination of diminution of temperature with the usual objective manifestations of heat is paradoxical but characteristic of thrombo-angiitis obliterans. The tips of the fingers may be slightly cyanotic or a cyanotic hue over the proximal portion of the nail bed is present.

The retracted sores at the tips of the fingers are apt to lie in whitened thinned-out skin, and although completely healed, are exceedingly sensitive to the touch.

With these manifestations the radial pulse may be absent in one or both hands. The circulatory manifestations do not bear the same relationship to posture as in the lower extremities, for ischemia may be absent on elevation, or if present, may be very slight.

In some cases the incipency of this affection in either the ulnar or radial arteries manifests itself in the coldness of one or more fingers only, and on examination one of these two arteries may be closed, one or two fingers distinctly cold, with a tendency to pallor. If an Esmarch be applied to the arm, the differences in circulation between the affected fingers and the others can be made more evident, for the reactionary hyperemia will be sluggish in appearing in the territory of impaired circulation.

A survey of many histories shows that the upper extremities may be clinically involved in the following ways: (I) without subjective symptoms; (II) with vasomotor symptoms predominating; (III) with lesions simulating the results of neurogenic disturbances; (IV) with trophic disturbances alone; (V) with trophic and vasomotor phenomena; (VI) with gangrene of slight extent; (VII) with extensive gangrene threatening the viability of the extremity; (VIII) with extensive atrophy of the hand and forearm; (IX) with changes simulating scleroderma and sclerodactyly; and (X) cases with acute arteritis of portions of the radial or ulnar artery (migrating arteritis).

I. Thrombo-angiitis Obliterans of the Upper Extremities without Symptoms.—Just as in thrombo-angiitis of the lower extremities, there are cases in which the radial or ulnar artery, or both, become gradually closed without the patient's experiencing any noticeable symptoms. In some instances, absence of pulsation was discovered during a routine physical examination; in others, where symptoms were present in the lower extremities investigation of the radial and ulnar vessels had demonstrated their occlusion.

J. A., male, aged forty years, Russian, began to have trouble in the right leg ten years ago (1904), pain coming on during walking, subsiding when at rest. Gangrene of the little and of the big toes developed, leading to amputation of the left leg at its middle in 1906. Since 1908, similar symptoms involved the left leg, and the first and second toes became ulcerated, also requiring amputation. During the period of clinical observation the right radial pulse gradually disappeared, although no vasomotor or trophic manifestations could be elicited on examination. The patient was lost sight of so that the further course could not be followed.

The symptoms of Raynaud's disease, too, may be closely mimicked, as in the following cases:

II. Cases in Which Vasomotor Phenomena Preponderate.—Such an instance is described in the following history, where, after about ten years of migrating phlebitis, and the usual circulatory disturbances of the lower

extremities, distinct evidences of involvement of the vessels of the arm and hand supervened.

The following history denotes an instance of remarkably striking vasomotor manifestations that are either part of the thrombo-angiitis obliterans syndrome or coincident with it. When we are confronted with neurotic manifestations suggestive of chronic acroasphyxia as here, a long period of clinical observation may be required in order to determine accurately whether two types of vascular disorder, neurogenic and organic obstructive are not simultaneously represented. Certain it is that vasomotor phenomena may accompany thrombo-angiitis obliterans as a part of the latter's symptom-complex.

J. V., male, aged thirty-four years, Russian, admitted to the hospital December 17, 1907, says that three and a half years previously he noticed that his fingers were cold but not blue. The following winter the same symptoms returned, but, in addition, the skin of the tip of the right middle finger became dry and a "wound" spontaneously developed. For the past two years his hands would get blue, cold, and numb on exposure to cold, their natural color returning in a warm room. There was never any pallor. A sort of "sticking" pain in the finger tips would regularly accompany the state of blueness.

Physical examination, December 17, 1907. Both hands are deeply cyanotic up to the wrist, and very cold. During the examination bright red or crimson colored spots can be seen to appear in the dorsum and palm. Over the back of the hand these red blotches become very distinct and do not shade off into the blue areas. The two distal phalanges remain deep blue. If the hands be observed for a still longer time (five minutes) the red color becomes paler and is mottled with a yellowish pink; at times a totally different and much lighter shade, variegated with red and blue, will completely replace the deep colors first noted. In the palm the red areas are not so apparent, but they also give way at times to the lighter shades. The terminal phalanges of the ring fingers are enlarged, those of the middle fingers somewhat less so. When the hands are held above the head for two or more minutes the redness disappears, a pale sickly purple remaining. The radials and brachials pulsate well.

In the lower extremity a similar picture is present, but there are evidences of obliteration of the vessels. The right dorsalis pedis cannot be felt, although palpated on many occasions from December 17, 1907, to January 20, 1908. In the left dorsalis pedis there is fair pulsation. There is ischemia in the elevated position of the legs, as evidence of the impaired vascular supply, and bespeaking the presence of the lesion, thrombo-angiitis.

If such an exquisite example of vasomotor disturbance can belong to a case of thrombo-angiitis obliterans, there is little wonder that confusion should exist in the differentiation of the symptoms due to neurogenic and organic vascular affections.

A. B., male, aged thirty-one years, Russian, noticed the appearance of small hard lumps under and in the skin of the calf of both legs in 1904 (ten years ago). They were painful, lasted for a few days or a week or more, and would then disappear (migrating phlebitis). For three years similar lumps and strands would come and go over the lower and inner side of the right thigh. About seven years ago he began to experience cramp-like pain in the right foot and calf of the leg on walking. Later the right foot became "cold." An ulcer developed on the third toe and showed no tendency to heal.

For seven years he has been suffering with similar symptoms in both legs and feet, the typical symptoms of pulseless vessels, erythromelia, ischemia in the elevated position, and gangrene of several toes being present. He now (1914) has already lost four toes of the left foot and two of the right.

Four months ago his right hand began to trouble him. In cold weather it would become very pale, particularly the little finger. On warming the hand, color would gradually return. Of late, however, the tip of the little finger has been bluish for days at a time, although excessive heat seems to bring back a normal color.

Physical examination, May 6, 1914. The radial and ulnar arteries of both sides pulsate distinctly. Both hands perspire profusely, and are somewhat cold. The tip of the little finger of the right hand is cyanotic and deeply discolored over its palmar aspect. Pressure over this part elicits some pain. Roentgen-ray examination of the hand is negative.

On July 31, 1914, patient says that the little finger and thumb of the right hand feel cold. Scales form on the tip of the little finger, and when these separate, leave a healed depression. He has no pain.

Physical examination shows that both the little finger and the thumb are distinctly cold to the touch, the coldness extending to the base of the fingers. The other hand and fingers are warm. The radial and ulnar arteries pulsate well. On elevation there is no appreciable change in the color of the fingers.

In short we have an example of thrombo-angiitis in which vasomotor symptoms initiate the onset of the disease in the upper extremities. Previous experience warrants the assumption that we may either expect a complete cessation of the symptoms in the hands, if adequate collaterals be established, or progressive occlusion of vessels until the radial and ulnar arteries become obliterated or until gangrene ensues.

III. Cases with Lesions Simulating Neurogenic Disturbances.—The following picture was characteristic in certain of the cases in which thrombo-



FIG. 49.—Atrophic and dystrophic changes in the fingers and nails in thrombo-angiitis obliterans.

angiitis obliterans of the lower extremities had already been present for a long time, necessitating amputation of one of the lower extremities.

All the fingers of the affected hand are tumefied and have an exaggerated conical appearance due to relative abnormal increase of the girth of the proximal portion of the fingers. The general swelling is such as to obliterate all of the normal furrows and markings. The texture and color of the skin also are altered in that portions of the skin, particularly about the nails, have a glossy appearance. The integument (Fig. 49) appears stretched over swollen subcutaneous tissues, and the color, too, is peculiar in that there is a diffuse reddening of the distal digits. There seems to be a subungual trophic disturbance manifesting itself by discoloration of the nails. As a result, the lunula is

increased in size to four or five times the normal. One or more of the fingers may show the absence of the distal portion of the last phalanx, and depressed scars, at the bottom of which a necrotic section of the bone may protrude.

The palmar aspect of the hand and fingers shows a general tumefaction and reddening. Both the radial and ulnar arteries usually fail to pulsate.

In addition to the objective manifestations, there *may be limitation of motion in most of the phalanges*.

In the case described below, the employment of hot baths, intermittent compression of the brachial artery was followed by rapid diminution of the edema and intensity of the rubor, and by improvement in the temperature of the fingers.

In rare cases there are atrophic changes in the bones of the hand associated with articular changes that do not show any evidence in the X-ray, but lead to ankylosis. The bone lesions differ from sclerodactyly in that there is no change in the terminal phalanges even though defects in the soft parts may occur. The most marked lesions in the bones are absorption and rarefaction of the radius and ulna and carpal bones, of the bases of the metacarpal bones, and of some of the phalanges.

The history in one of the typical cases was as follows:

R. L. was observed from July 23, 1912, till March, 1921. In January, 1912, he was twenty-nine years of age, with the usual symptoms of thrombo-angiitis obliterans of the left lower extremity, with the typical erythromelia, and absence of dorsalis pedis and posterior tibial pulsation. The process was progressive; on the 8th of March, 1918, it had advanced so as to involve both extremities. There had been ulcerations of the toes of both feet. The right leg was amputated in 1918. March 17, 1912 he consulted me because of severe pain in the right hand radiating to the wrist, and because of the discoloration of the nails and of the fingers. He says that the first sign of trouble in the right hand, was the absence of the radial pulse, which he felt repeatedly, having a good knowledge of the significance of pulsation, and fearing that the right hand might be involved. About eight months ago, spontaneous gangrene of the tip of the ring finger of the right hand occurred, and following this the other fingers became swollen and reddened.

May 5, 1921, rubor still present, but rather diminished. The opaque portion of the nail is greater than before.

The disappearance of such marked symptoms 18 months later is worthy of note; Oct. 26, 1922, remarkable improvement in the condition of the right hand, the chronic rubor having disappeared. The fingers have taken on a more healthy appearance, the only evidences of disturbance being the retracted scar at the tip of the ring finger of the right hand where a piece of bone had separated; and the somewhat atrophic condition of the skin. The right brachial artery can be felt beating in its upper part, but its pulse is imperceptible below the middle of the arm, although it is easily palpated. The left brachial artery can be felt all the way down. Just as remarkable as the disappearance of the chronic erythromelia and the normality of the nails and nail-beds, is the *freedom of motion in the interphalangeal joints*, in which the fixation 18 months previously seemed sufficiently advanced to threaten chronic ankylosis of the joints.

This pseudo-ankylosis appears at first sight to be due to joint involvement. However, it was observed to disappear in the following case, as the vasomotor and trophic disturbances gradually improved. Perhaps the fixation is of the nature of those sympathetic contractures that the French authors attribute to derangements of the periarterial sympathetic. The extensive obliteration of the radial and brachial arteries with the periarteritis that accompanies would seem to substantiate such a theory, although such contractures and fixations are but rarely observed.¹

Another striking instance of the association of vasomotor symptoms and trophic lesions is the following:

¹ See Chaps. LXXXVI, XCI, and CV.

A. W., 24 years, a Russian Hebrew, had thrombo-angiitis obliterans of both legs, necessitating amputation of the right leg.

November 8, 1922. For some weeks there has been pain in the fingers of the right hand, coldness, varying discoloration of the fingers, and an ulcer developed at the tip of the ring finger.

Physical Examination.—The right hand has a peculiar variegated appearance due to the difference of color in the various parts of the fingers, and the abnormal appearance of the nails of the second, third and fourth digits.

Color changes take place while under observation, in that parts of the fingers are deeply cyanotic, and other parts have a more scarlet hue; still other areas have a yellowish ashen tint. Over the tip of the fourth finger, near the nail-bed, there is necrosis of the skin and an accumulation of fluid under the adjacent skin, the whole region being deeply cyanotic. All the fingers are slightly swollen.

The radial and ulnar arteries do not pulsate, but the brachial artery can be felt down to the elbow. The pulses of the left hand are normal.

The *texture of the nails* is entirely changed, being completely whitened and having the appearance of celluloid or sea shell, this due to an opacity that does not permit the matrix to shine through. They seem abnormally convex and prominent.

IV. Cases with Trophic Disorders Only.—In some patients, distinctive signs of an affection of the upper extremities manifest themselves as trophic disturbances not extensive enough to lead to gangrene. The disease may be wholly overlooked by the patient and, when the lesion has healed, it may be subsequently referred to by him as a slight “sore” or “ulcer” developing without cause. Were it not for the presence of the disease in the lower extremities and for the changes in the radial pulse the nature of the trophic disorders would be difficult of solution.

T. S., aged thirty-one years, Russian, consulted me in May, 1914, because of the condition of his left foot. Three and a half years previously he experienced pain in the sole of the left foot on walking and was treated for rheumatism. Two years after the onset a sore developed between the fourth and fifth toes of the left foot and another one on the tip of the big toe of this foot. Since then the foot became red and the little toe gangrenous, falling off about a year ago. About this time his right leg began to trouble him, the symptoms being pain in the calf on walking.

Two and a half months ago there developed a spontaneous ulcer over the middle phalanx of the right hand, not accompanied by any evidence of inflammation, hardly painful, and not brought about by any injury. He was treated for this for about eight weeks, when the wound healed.

Physical examination, May, 1914. Over the middle phalanx of the right hand there is an irregularly shaped scar, about 8 mm. in length and 4 mm. in width, evidently the site of the old healed lesion. The right radial pulse is not perceptible.

We have here a typical case of thrombo-angiitis of the lower extremities, first involving the left then the right lower extremity, and three years later manifesting itself also in the hand, with trophic disturbances and obliteration of the radial artery.

V. Cases with Trophic and Vasomotor Phenomena.—It is rather characteristic of the symptomatology of the disease as it affects the upper extremities that manifestations are frequently overlooked by the patient, until definite objective signs, such as trophic ulcers, make their appearance. The almost inexplicable development of such phenomena may lead to careful examination on the part of the physician, and to the detection of the absence of the radial or ulnar pulse, or even the brachial. The chronological sequence of events in a number of these cases is the following:

(1) Symptoms of thrombo-angiitis obliterans of the lower extremities, with or without amputation of one extremity, or ulcers of both, over a period.

(2) A stage of involvement of the upper extremities with ulcers, and disappearance of the pulses in this territory.

(3) A chronic period with more or less permanency of symptoms both in the lower and upper extremities, a condition of vasomotor lability and impaired circulation of the hand being a striking development.

S. S. S., 37 years, born in Russia, consulted me on the 19th of September, 1922, with a history of having had an amputation of the left leg, and complaining now of pain in the right foot; inability to walk, ulcers of the big and little toes, coldness, discoloration of the foot; also of numbness of the tips of the fingers of both hands, and a chronic fissure or ulcer on the middle finger of the right hand.

Six years ago he began to experience pain in the left foot, and phlebitis was recognized. In 1918 a diagnosis of occlusion of the blood vessels of the left leg was made. After the removal of a callous a wound developed, which did not heal, and the foot became progressively worse. He was treated until September, 1920, when amputation of the left leg had to be performed.

In October, 1921, the right foot began to annoy him, and shortly thereafter ulcers developed over the big and little toes of the right foot. In January, 1922, the big toe became bluish and the wound was still not healed. Then improvement occurred, but another ulcer developed 3 weeks ago on another toe, and the foot became very painful.

The History of the Upper Extremities.—As far as he knows there were no symptoms referable to the upper extremities until January, 1922, when ulcers developed at the tips of the second and third fingers of the left hand. Since then, however, both hands became *numb* and *cold*, and bluish discoloration has been regularly noted in cold weather; latterly even at room temperature. Within the last 2 weeks he complained of numbness of the right hand. However, as far back as January, 1922, he was told that the ulnar and radial pulses of both hands were not palpable.

In short, an old history of thrombo-angiitis obliterans of both lower extremities followed by the development of ulcers on the tips of the second and third fingers, closure of both ulnars and radials having already been present, when the ulcers appeared.

Physical Examination.—On the left there is a stump, amputation having been performed above the knee. The right leg is in a condition of intense erythromelia, both the dorsalis pedis, posterior tibial and popliteal pulses being absent. The right and left femorals pulsate. The coldness of the foot extends up almost to the ankle.

The Upper Extremities.—The tips of all the fingers are markedly cyanotic, particularly those of the left. The lividity extends almost to the bases of the first phalanges over the volar aspect of the left hand, and not quite so far centrally on the dorsal aspect. The cyanosis is less marked on the right. The fingers are cold, as far as 1 inch beyond the metacarpal phalangeal joints on the left, and up to the metacarpal phalangeal joints of the right hand. Both ulnars, both radial, and the right brachial arteries do not pulsate. The left brachial pulse is small.

On elevation of the hands there is a moderate degree of blanching, but the cyanosis is exaggerated in this position. The tips of the index and middle fingers of the right hand show cicatrices and retracted fissures near the nails. Similar, but less marked lesions are present in the same situation in the left hand. Both hands show marked reactionary rubor after preliminary elevation, especially the right hand.

Comments.—It is rather noteworthy that in spite of the extensive obliteration of the arteries of the upper extremities here, such minimal trophic disturbances should have developed. As contrasted with the appearances of the lower extremities in such cases, and as well illustrated in this case, the intense cyanosis may characterize the upper extremities, whilst a marked degree of rubor is present in the foot or feet. That vasomotor phenomena play a rôle in producing the exaggerated lividity, seems evident, for variations in the degree of asphyxia frequently occur, and much of it may disappear and give way to reactionary erythromelia when the arms are elevated and depressed secondarily for a number of times. Whether a venous spasm plays a rôle is worthy of investigation. The intensive asphyxia of the hands in some of these cases might lead to the tentative diagnosis of chronic acroasphyxia, if careful attention is not given to palpation of the pulses.

VI. Cases with Gangrene of Slight Extent.—Not a small number of the patients that suffer with occlusion of the vessels of the upper extremities come to us with a history of having had pain in the tip of one of the fingers

for a considerable time. This is followed by a change in the color of the skin, usually reddening of the tips of the fingers, as if they were inflamed. Later there develops a sore or the skin changes color and becomes gangrenous, usually at the tip of a finger, although the lateral margin of the finger may be first affected.

M. S., aged forty-seven years, Russian, was admitted on June 25, 1907, giving the following history: About eight or nine months ago he noticed that the fourth toe of the left foot was cold, blue, and painful. About four months ago the pain became so severe that he consulted a physician, who told him that an infection had taken place. Since this time a sore developed under the nail and the nail-bed became black.



FIG. 50.—Gangrene of the tip of the index finger.

Physical examination showed complete gangrene of the distal half of the fourth toe of the left foot, absence of pulsation in the dorsalis pedis artery, an area of superficial gangrene of the skin on the dorsum of the foot, intense erythromelia (hyperemia of the foot) in the dependent position, and marked ischemia in the elevated position. June 28, 1907, amputation was done through the tarsometatarsal articulation. On July 5, re-amputation was done through the middle third of the leg, the wound healing slowly.

In 1910 the disease began to involve the right leg in the same typical manner, leading also to dry gangrene of the fourth toe. When examined in March the popliteal, posterior tibial, and dorsalis pedis of the right leg could not be felt.

In short we have a typical case of thrombo-angiitis obliterans, first involving the left lower extremity leading to gangrene, amputation, and some three years later involving the right leg.

In March, 1914, I again saw the patient, who now complains of symptoms in the left hand.

March 18, 1914. For several months he has had pain in the tip of the left index finger and lately the finger has changed color becoming withered and glossy.

Physical examination shows an ulcer at the tip of the left index finger, the live skin above it atrophied and glossy, the hand somewhat smaller than the other, and the fourth finger of the same hand distinctly shrunken. The radial pulse of this hand cannot be felt (Fig. 50).

We are evidently dealing here with a case in which some seven years after the onset of the disease in the lower extremities, the left upper extremity became attacked, as evidenced by ulceration and trophic disturbances.

An interesting group is formed by those patients in whom trophic disturbances and gangrene are the salient features. These are the cases so often confused with Raynaud's disease. The lower extremities are regularly involved at some time or other, and it is, therefore, necessary to watch carefully for the advent of the typical symptoms in these, so that a correct interpretation of the phenomena in the fingers and hands may be made. The following two histories will well illustrate.

VII. More Extensive Gangrene.—The gangrene is usually of very limited extent and confined to the tips of the fingers. However, it may progress so as to involve the whole of several fingers and be accompanied by such signs of circulatory impoverishment as to arouse the fear that the hand or forearm may be lost.

A. K., male, aged twenty-seven years, Russian, was admitted to Mt. Sinai Hospital, January 4, 1908. About two years previously he had had severe pain in the middle finger of the right hand. The finger became cold, at times very blue, and extremely painful. These symptoms persisted for about two months, when he was told to have the nail removed. Shortly after this was done the tip of the finger became dry and black. After several months the terminal phalanx separated spontaneously, but a wound remained which refused to heal.

For about two months his left hand has been affected, there being excruciating pain in the middle finger of the left hand, and the fourth finger of the right hand also being somewhat painful. He thinks that the tip of the middle finger of the left hand first became dark blue or purple, and lately has become dry and black.

Physical examination, January 4, 1906, shows that the distal phalanx of the middle finger of the right hand is absent, the tip of the fourth finger of the left hand showing a small patch of dry gangrene and there is beginning gangrene of the distal phalanx of the middle finger.

Somewhat more than a year later, February 24, 1907, he was again admitted to the hospital, presenting evidences of thrombo-angiitis of the left foot. The second toe of the left foot had been ulcerated for about three months, and gradually all the toes of that foot, except the fourth, became involved in the same process.

Physical examination, February 24, 1907. Left foot: On the dorsal and plantar surfaces of the great toe there are ulcers. A similar condition is found at the tip of the second toe and on the plantar and dorsal surfaces of the fifth toe. The skin about the ulcer is sloughing and shows no tendency to heal.

The right foot is negative. The right hand shows an absence of the terminal phalanx of the third finger. Both hands are cyanosed.

March 22. Amputation of the toe. Wound does not heal.

May 17. Re-amputation through the leg.

Physical examination, May 20, 1907. The left radial pulse is absent and the artery appears to be converted into a hard cord. In the right radial artery a very faint pulse is perceptible. The brachial artery seems to be much thickened, although the pulsation is good. Ever since amputation of the left leg was done, the stump was painful, discolored, bluish, presenting a wound that failed to heal. Finally, on January 2, 1909, the patient consented to re-amputation. The author performed the Gritti-Stokes amputation, the stump healing kindly.

January 3, 1909. The tip of the little finger of the right hand presented a small spot of gangrene about 1 cm. in diameter. The distal phalanx of the third finger is absent. The nail of the fourth finger is deformed and thickened. In the dependent position the fingers become cyanotic, with a slight increase in the normal red color. The left hand is normal as regards color, but the nail of the middle finger as well as the tip are very much deformed.

The right radial artery is felt as a cord, and no pulse can be detected; the ulnar artery is also pulseless; the brachial pulse is poor. The left radial artery is faint, the ulnar cannot be felt, the brachial also is poor. In the elevated position the right hand becomes somewhat paler than the left, but neither becomes very much blanched.

Lower extremity: The stump is in good condition. The right foot shows evidences of development of thrombo-angiitis, the dorsalis pedis and posterior tibial arteries being absent, and there are other evidences of involvement of that leg.

December 30. The fifth finger of the right hand presents an ulcer at the tip, the result of the separation of a gangrenous patch. He says that he has had pain in that finger for about three months, and that gangrene set in about three weeks ago.

February, 1910. The trophic disturbances, involving the little finger of the right hand seem to be progressive. The tip of the finger shows advancing gangrene, the rest of the finger is swollen and red. In the dependent position the third and fourth fingers become intensely red and slightly cyanotic. Left hand: Here there has been no progression of the symptoms.

February 2, 1910. The little finger of the right hand was amputated (Fig. 51).



FIG. 51.—Necrosis of the tip of the middle finger of the left hand; results of amputation of the fingers of the right.

This is a good illustration of those cases of thrombo-angiitis obliterans in which the symptoms first make their appearance in the upper extremities, are initiated by pain, and followed by trophic disturbances and gangrene. In this case the terminal phalanx of the middle finger and the whole of the little finger of the right hand were lost. During the evolution of these symptoms the disease attacked the left leg, where even greater progress was made than in the upper extremities, amputation being the outcome. Pathological examination of the vessels of the amputated left limb showed the usual lesions of thrombo-angiitis obliterans.

VIII. Atrophy and Gangrene.—It is rare that gangrene of the fingers and hand becomes so extensive as to warrant amputation of the forearm or arm. In neglected cases with secondary infection, however, such may be the issue. Interesting, indeed, is the occurrence of extensive gangrene of one upper extremity and atrophy of the other as results of the vascular obliterative process in the following case.

S. A., male, Russian, examined March 23, 1905, records a typical history of thrombo-angiitis obliterans of the left lower extremity, finally leading to gangrene, for which the leg was amputated August, 1903, and re-amputated September 5, 1903, at the knee.

Eight weeks before admission there appeared symptoms referable to the same disease of the right lower extremity, an ulcer appearing at the inner side of the right heel. On March 21, 1905, the right leg was amputated for advancing gangrene of the right foot.

March 10, 1910. I found evidence of the involvement of the left upper extremity. He says that he has had trouble in his left arm and in the fingers and forearm for several months, there having been pain in the fingers, followed by swelling and redness. Then a bleb appeared at the tip of the index finger, which was incised by a physician. Shortly after this the wound became much worse and sloughing took place. About the same time a black spot appeared over the back of the middle finger. Neither middle nor index finger has improved, and it is for these that he seeks relief.

After admission the gangrene rapidly spread, the pain becoming excruciating, and the forearm was amputated through its upper fourth.

The ablated forearm (Fig. 52) showed complete occlusion of both radial and ulnar arteries. The typical lesions of thrombo-angiitis obliterans were present.



FIG. 52.—Amputated arm (photographed after fixation) showing extensive gangrene of index finger.

Four years later, April, 1914, the patient was again admitted in a condition of stupor. The notes taken read as follows: "Both legs and the left arm have been amputated. Speech is incoherent and there are evidences either of some cerebral lesion or of an arterial lesion in the brain. The condition of the right hand is of particular interest. Nowhere is there any evidence of ulcer or gangrene. *The skin of the right hand is dry and atrophic. The fingers have a tapering appearance. The skin has lost its elasticity, the subcutaneous tissues have withered, and neither the radial nor the ulnar arteries are palpable.* The brachial artery, too, gives but the slightest impression of the presence of pulsation."

Here, then, is a case in which two distinct clinical pictures were evolved in the course of the obliterative vascular disease, one exhibiting gangrene of

an upper and two lower extremities, and the other demonstrating the unusual phenomenon of extreme atrophy of both hand and forearm.

IX. Cases Simulating Scleroderma and Sclerodactyly.—Perhaps most interesting of all are those cases in which the vascular occlusion has led, by virtue of the effects of malnutrition, to a condition of dystrophy, the clinical picture being akin to that of sclerodactyly. In fact we have had occasion to observe a most pronounced example of this manifestation in a patient in whom the diagnosis of scleroderma was made by expert dermatologists.

I. L., aged thirty-five years, was admitted on October 1, 1906, with a typical history of thrombo-angiitis obliterans of the left leg. There was absence of pulsation in the dorsalis pedis and complete gangrene of the second toe, necessitating amputation of the leg. Pathological examination of the vessels of the amputated leg showed the typical lesions of thrombo-angiitis obliterans.

June 29, 1907. He was again admitted to the hospital, complaining of intense pain in the right leg which showed the symptoms of ischemia on elevation, redness in the dependent position, but no evidence of trophic disorder or gangrene. The patient begged that the limb be taken off, and the right leg was, therefore, ablated through the middle third. Pathological examinations showed here, too, the typical lesions of thrombo-angiitis obliterans.

December 17, 1909. He entered the hospital complaining of trouble with his right hand and arm. For several months he has been unable to use it properly, the muscles having become stiffened. He thinks, too, that a marked diminution of the size of the hand and arm has taken place.

On physical examination the picture presented by the right arm is striking. The fingers have the typical appearance of the skin in scleroderma. Motion of the distal phalangeal joints is markedly impaired in extent. The skin is atrophic and dry and the circumference of the fingers of the right hand is distinctly diminished. Both the radial and brachial pulses are absent. The brachial artery can be felt as a hard cord, and can be traced as far as the axilla. In the axilla there is a distinct pulse.

The left hand shows no trophic disturbances, no ulcers, but the radial and ulnar pulses are absent. The brachial pulse is fairly good.

X. Cases with Acute Arteritis of Portions of the Radial or Ulnar Artery (Migrating Arteritis).—Just as a single or limited number of tributaries of the veins of the forearm may be the seat of an acute thrombo-phlebitis, and antedate the signs of the deep seated process by months or years, so also restricted portions of the radial or ulnar artery may be come suddenly acutely inflamed, adherent and thrombosed. An interesting example where that portion of the course of the radial artery immediately above the wrist was involved, is the following.

H. S., Russian, male, 38 years old, complained of burning pain in the thumb, index and middle fingers of the right hand, also of swelling and reddening over the course of the radial artery for the past 4 months. There were no symptoms in any of the other extremities.

Upon physical examination the right radial artery could be felt as a thickened cord, and occluded up to a point $2\frac{3}{4}$ inches above the wrist. There was no ischemia, and the radial pulse was absent.

The specimen of the right radial artery after resection showed the following.

Pathological examination: There was intensive periarteritis and marked thickening of the vascular sheath and overlying fascia. When the latter was opened over the groove director, the radial artery was firmly adherent and could only be liberated with difficulty. About $3\frac{1}{2}$ inches were removed. The lower end did not bleed on section, and showed the typical lesions of rather advanced thrombo-angiitis obliterans in the brownish stage. The upper end of the clot was darkish red, lying in a contracted but *patent vessel* $1\frac{1}{2}$ inches above the wrist. There must have been another thrombotic lesion higher up, since bleeding did not occur. It is, therefore, permissible to call the process a migrating one. The absence of pulsation in the patent portion was doubtlessly due to a similar occlusive process centrally situated.

Microscopic examination confirmed the diagnosis.

Another instance of thrombo-arteritis involving the radial and ulnar arteries of the right forearm, and a portion of the left radial artery, is illumin-

ating in demonstrating the close relationship between the advent of circulatory disturbances and tenderness along the course of the right radial artery.

T. G. H., American Gentile, 45 years of age, states that 8 years ago he had had symptoms of intermittent claudication of the right leg, followed by similar symptoms of the left. The history suggests that there had been migrating phlebitis of the lower extremities. Ulceration of the right big toe 5 years ago; subsequently similar symptoms in the left foot, and gangrene of both; 2 years ago amputation of both legs at the upper fourth. Three and one-half months ago there developed numbness of the tips of the fingers of the right hand, with tenderness and vague pain along the course of the right radial artery from the wrist to the upper fourth of the forearm, with disappearance of the right radial pulse 1 month after the onset of the symptoms. The right ulnar artery disappeared almost simultaneously with the right radial.

Physical examination, January 22, 1923: The fingers of the right hand are colder than those of the left; the radial and ulnar pulses absent; moderate ischemia on elevation, marked reactionary rubor; tenderness along the lower half of the right radial artery. The left radial artery is absent at the wrist, the ulnar pulsates; vasomotor instability of the right hand.

CHAPTER LX

THROMBO-ANGIITIS OBLITERANS—ASSOCIATED ARTERIOSCLEROSIS

The clinical picture of thrombo-angiitis obliterans becomes confused when it is complicated with arteriosclerosis. In most of the cases the patient must have had either the insidious or silent form of thrombo-angiitis obliterans which developed gradually with only an indefinite history of intermittent claudication. These are followed by spontaneous cure so far as evidences of impaired circulation are concerned. Later, between the ages of 50 and 65 or even older, either because of the gradual occlusion of the collateral vessels by the atherosclerotic process, or by virtue of a recent thrombosis complicating the arteriosclerosis in the popliteal artery or higher, the symptoms of insufficient circulation return, often very rapidly, and gangrene may result. In such patients we are apt to find not only pulseless vessels on the affected side, but also in the limb which shows no symptoms.

Or, more rarely do we find thrombo-angiitis obliterans developing rather late as far as can be determined by the anamnesis; then a period of temporary recovery, followed later on by recurrence of the symptoms in arteries markedly sclerosed or calcified.

The pathological investigation of the arteries in such cases has demonstrated two lesions side by side, that of the arteriosclerosis with its degenerative sequelae, and that of thrombo-angiitis obliterans (Fig. 124).

Occasionally we encounter the precocious development of arteriosclerotic patches in arteries that are the seat of thrombo-angiitis. We need not wonder at this circumstance, since it is not uncommon to find marked atherosclerosis in relatively young individuals in whom thrombo-angiitis is never a complication. Nevertheless it must be admitted that a predisposition to vascular disease (vascular mediocrity or inferiority) as it manifests itself in certain cases, seems to express itself both in a susceptibility to thrombotic lesions as well as to degenerative ones. Certain it is that the autopsy findings in cases of thrombo-angiitis show that the more centrally

situated arteries do develop a tendency to atherosclerotic lesions even though the arteries of the extremities show but little sclerosis.

For diagnostic and pathological data the reader is referred to the chapters on Arteriosclerosis, Pathology, and Diagnosis of Thrombo-angiitis Obliterans.

Clinically these cases fall into the following groups:

1. Cases with undiscovered thrombo-angiitis that had been present during the early years of maturity (from the ages of 20 to 40), but in which vague aches in the limbs, difficulty in walking, and similar symptoms, were insufficient to lead to a diagnosis. In these patients the disease remained in an arrested or non-progressive state.

2. Cases in which such a latent period as above described is followed by a moderate degree of arteriosclerotic change in the arteries of the extremities as the individual grows older.

3. Cases in which the latent thrombo-angiitis is followed by intensive arteriosclerosis.

4. Cases in which either relapsing thrombo-angiitis or bland thrombosis in arteriosclerotic vessels leads to gangrene in elderly individuals.

CHAPTER LXI

THROMBO-ANGIITIS OBLITERANS—PATHOLOGY

Thrombo-angiitis obliterans has been previously described by the Germans under the name "Spontan-Gangrän" and "Endarteritis Obliterans." In 1879, von Winiwarter published the results of the pathological findings in one case, and reported on obliteration of practically all of the arteries of the leg by reason of a chronic proliferative process due, in his opinion, to a new growth of tissue from the intima. He, therefore, proposed a new name for this condition, namely, "Endarteritis Obliterans."

This theory has been accepted by most authors, and even to-day, it is to be found in many text books. Somewhat later, Wilonski pronounced the opinion that the essential change in the vessel walls was due to a multiplication of the elastic fibers, and proposed the name "Arteritis Elastica" for the condition. Perhaps the most important contributions are those of Weiss and Zoege von Manteuffel, because these authors placed an entirely new interpretation upon the pathological findings. Basing his paper upon the studies of his assistant, Weiss, von Manteuffel suggests that the extensive occlusion of the vessels in this disease is dependent upon a primary arteriosclerosis; that the obliterative process commences in the popliteal artery, where it owes its inception to the formation of a parietal white thrombus; and that by virtue of a gradual extension of the parietal thrombus downward, followed by organization, a picture resembling an obliterative endarteritis is produced. In his cases the veins did not seem to be involved in the process. Von Manteuffel comes to the conclusion that the thrombosis is due to desquamation of endothelial cells, and that this occurs where the intima shows most advanced lesions of arteriosclerosis, namely, somewhere in the popliteal artery.

In 1908 the author pointed out that the name, endarteritis obliterans, as applied to the clinical picture just described, should be discarded, since the occlusive lesion is a thrombotic one, affecting arteries as well as veins of the

extremities, and that it is independent of athero- or arteriosclerosis. He proposed the name, *thrombo-angiitis obliterans*, which has now found almost universal adoption in English speaking countries.

Investigations¹ which included a thorough pathological and histological study of the vessels in 45 amputated lower extremities, 1 upper extremity, and 25 pieces of superficial veins resected and exsected from the lower and upper extremities during attacks of so-called migrating phlebitis, have demonstrated that when the patient comes to the physician for observation, the larger arteries and often the larger veins, are completely obliterated.

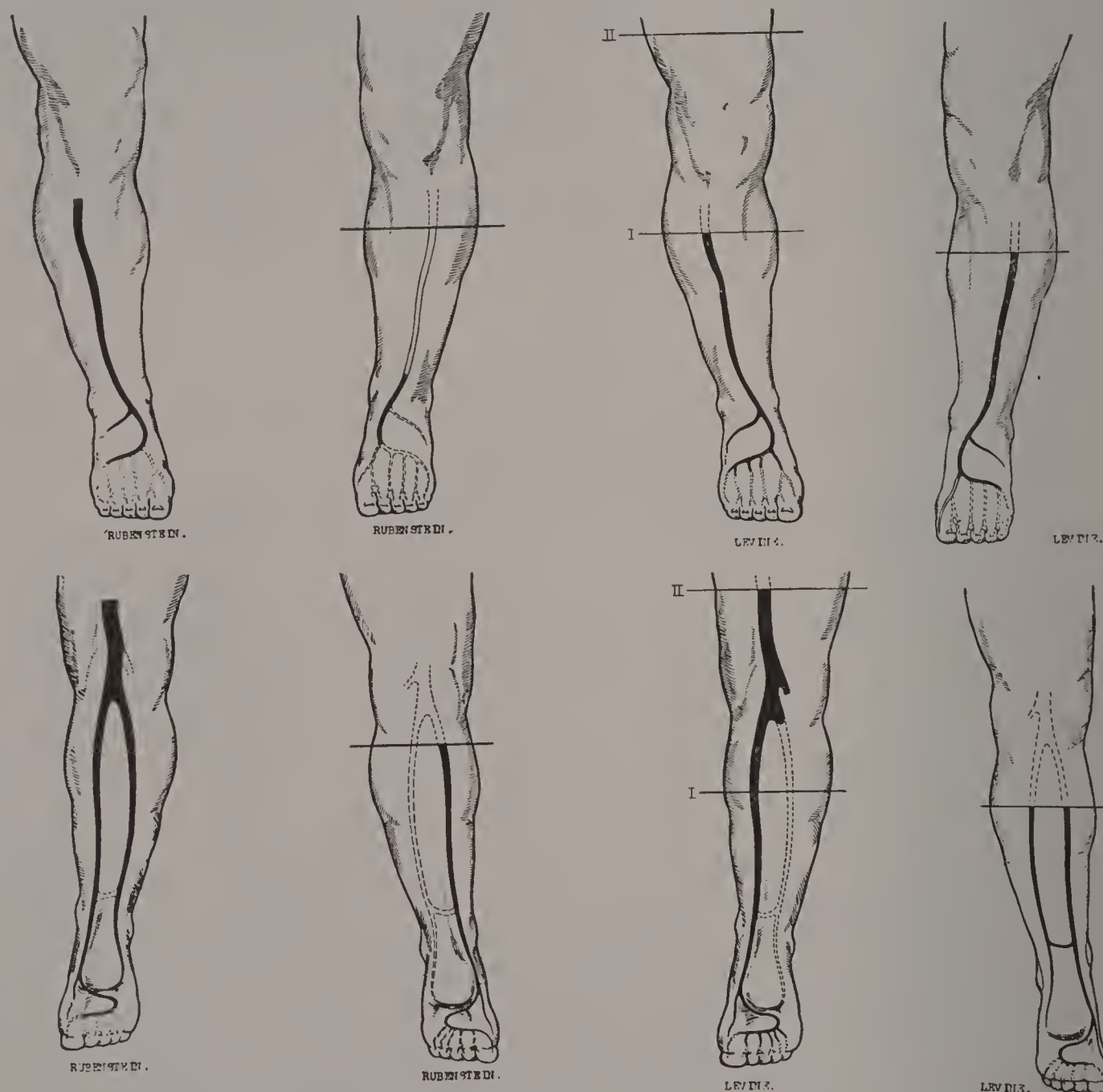


FIG. 53.—Schematic drawing showing the extent of occlusion in the arteries of the lower extremities in thrombo-angiitis obliterans. The cross lines represent the points at which amputation was done, I indicating the first amputation; II, reamputation. The anterior vessels are shown above; the posterior, below. The dotted lines indicate that the vessels were not examined. The four sets will be referred to in the text as 53 a, b, c, d, from left to right.

In the Figs. 53, 54, 55, 56, 57, 58 and 59 a schematic representation of the extent of occlusion in the larger vessels of 29 amputated lower extremities is

¹ Buerger, Am. Jour. Med. Sc., Oct., 1908. Proc. New York Path. Soc., Feb. and March, 1908. Int. Clin., III, 19th series, 1909. Jour. Med. Res., Nov., 1914, XXI, No. 2. Am. Jour. Med. Sc., Feb., 1915, p. 210.

shown. Examinations were conducted below the horizontal lines indicated in the drawings, and if a second amputation was performed, again in the region between two horizontal lines.

A very extensive obliterative process was found in Fig. 53*a* where all of the larger vessels from the beginning of the popliteal downward, were completely

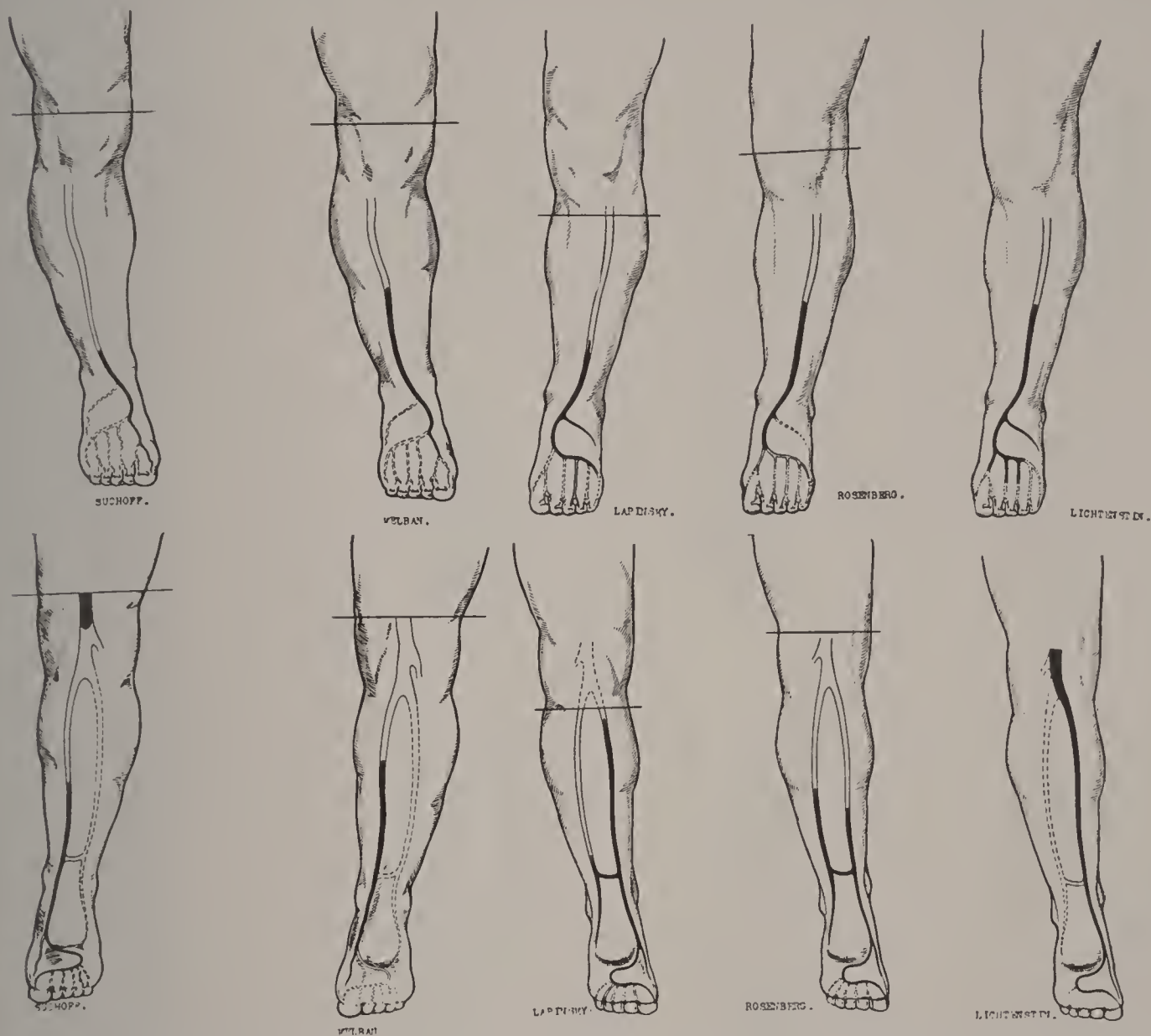


FIG. 54.—Schematic representation of extent of occlusion in thrombo-angiitis obliterans; referred to as *a*, *b*, *c*, *d*, *e* from left to right in the text.

obliterated. In Fig. 53*b* upper part of the anterior tibial artery was open as depicted, although the posterior tibial and plantars were obturated. The sharp lower end of a thrombus is seen in the upper peroneal artery in Fig. 53*c*, this being the only one of the larger arteries to remain intact.

Popliteal thrombosis with patent peroneal and upper posterior tibial arteries, is exemplified in Figs. 54*a* and 55*c*. In Fig. 54*b* and *c* the upper extent of the process was detected in each case. More complete involvement of the posterior tibial and popliteal arteries was presented by other cases Figs. 54*e*, 55*a* and 59*c-d*.

The thrombotic lesion in the popliteal may extend down into the anterior tibial, ending abruptly a short distance below the aperture in the interosseous membrane (Figs. 56*a* and 57*a*), leaving certain portions of the anterior tibial open.

Sometimes the posterior vessels except for the plantars are unaffected (Fig. 57c) and then again we meet those in which the anterior vessels are almost free, except for their most distal branches. Completely patent anterior tibial arteries are shown in Figs. 58a and b; partly open in 58c and d.

Where the vessels are dotted, their course was not thoroughly examined.

As a rule, the plantar vessels, dorsalis pedis and many of its branches, anterior tibial, posterior tibial, peroneal, and sometimes the popliteal are already completely closed, although any one or more of these vessels may

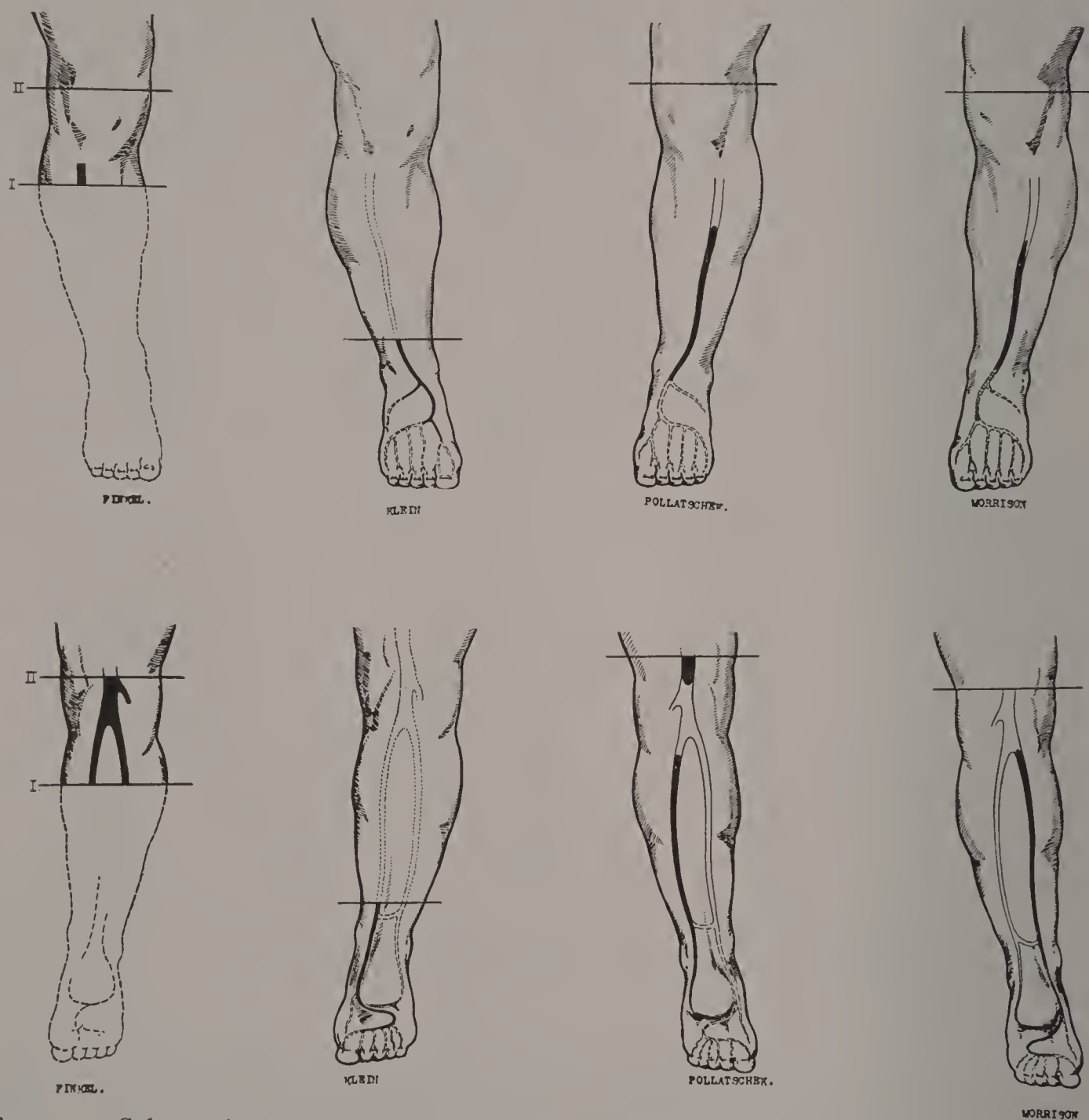


FIG. 55.—Schematic representation of extent of occlusion in thrombo-angiitis obliterans, (a, b, c, d from left to right).

escape. One or both the venae comites may partake of the same lesion. The obturating tissue is, for the most part representative of, or indicative of a healed lesion, or the end-stage of a process, whose incipency is marked by an acute inflammation of the vessel wall, with consecutive, red, occlusive thrombosis of the affected vessel. It is only in rare instances that the early stages of the vascular lesion are found in the deep vessels, but in superficial veins, when they are affected with the lesion migrating or thrombo-phlebitis, the early or acute stage of the disease can be studied.

The author has observed what he terms the acute lesions of the disease in territories other than the vessels of the extremities, namely, *in the spermatic artery, in the veins of the spermatic cord; and old lesions in one of the branches of the gastric artery in a case of ulcer of the stomach.*

Gross Pathology.—The deep vessels of the amputated legs regularly show an extensive obliteration of the larger arteries and veins. Besides this, there are two other lesions which vary greatly in their intensity, namely, the peri-

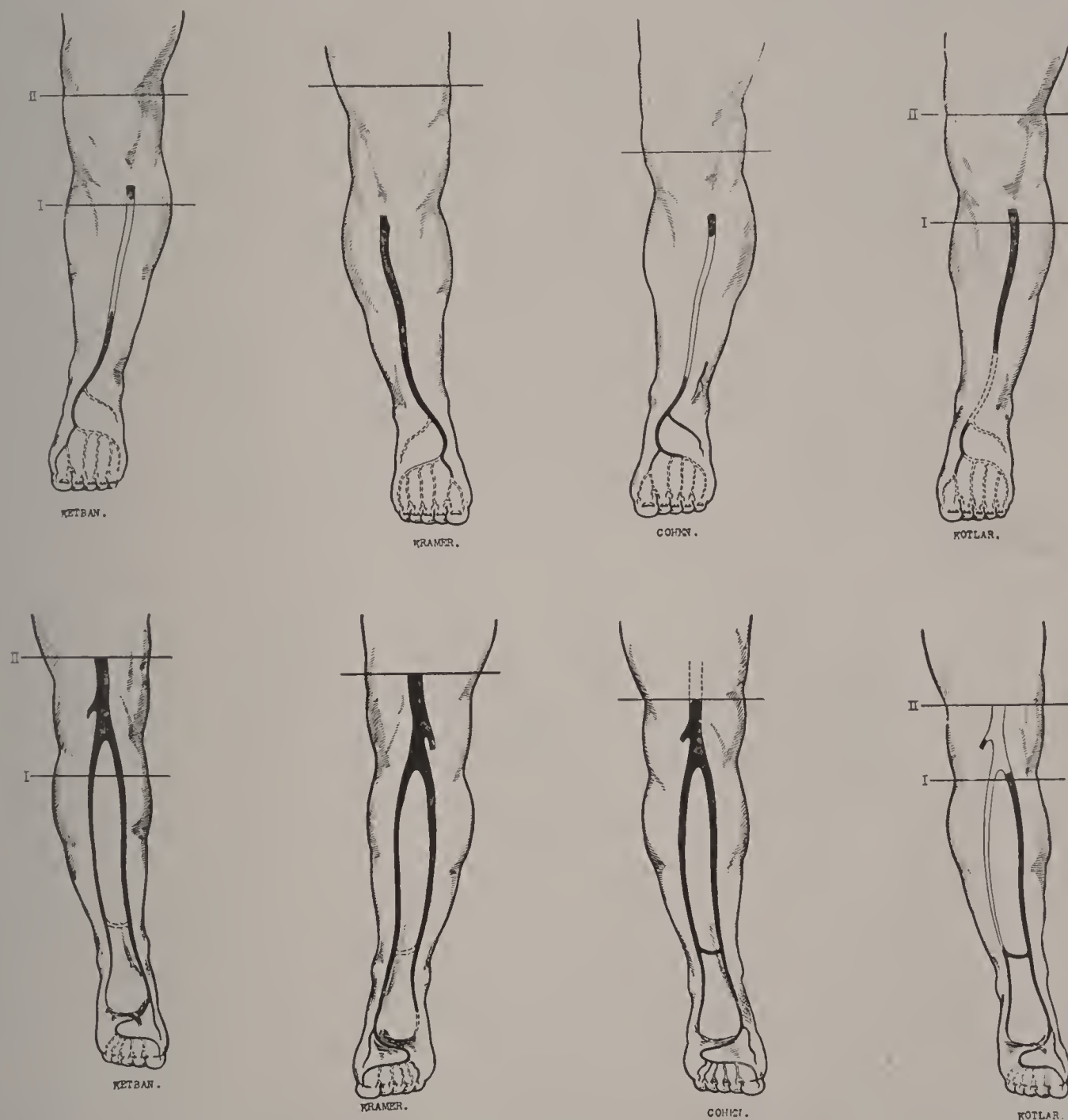


FIG. 56.—Schematic representation of extent of occlusion in thrombo-angiitis obliterans, (a, b, c, d from left to right).

arteritis and the arteriosclerosis. The appearance of the vessels on gross section depends upon the age of the occluding process. Usually the vessel is seen to be filled with a grayish or yellowish mass that can be distinctly differentiated from the annular wall of the vessel, and that appears to be pierced at one or a number of points by an extremely fine opening, through which a minute drop of blood can be squeezed. Such obturating tissue is firm in consistency, and does not at all resemble the crescentic or semilunar occluding masses typical of arteriosclerosis. The vessel itself is usually con-

tracted, so that its wall appears somewhat thickened. This picture is characteristic of arteries or veins which are the seat of a very old obliterative process, and is to be found most frequently in the peripheral portions of the vessels, although at times this type of lesion may extend throughout the whole length of the vessel, from the *dorsalis hallucis* into the popliteal artery.

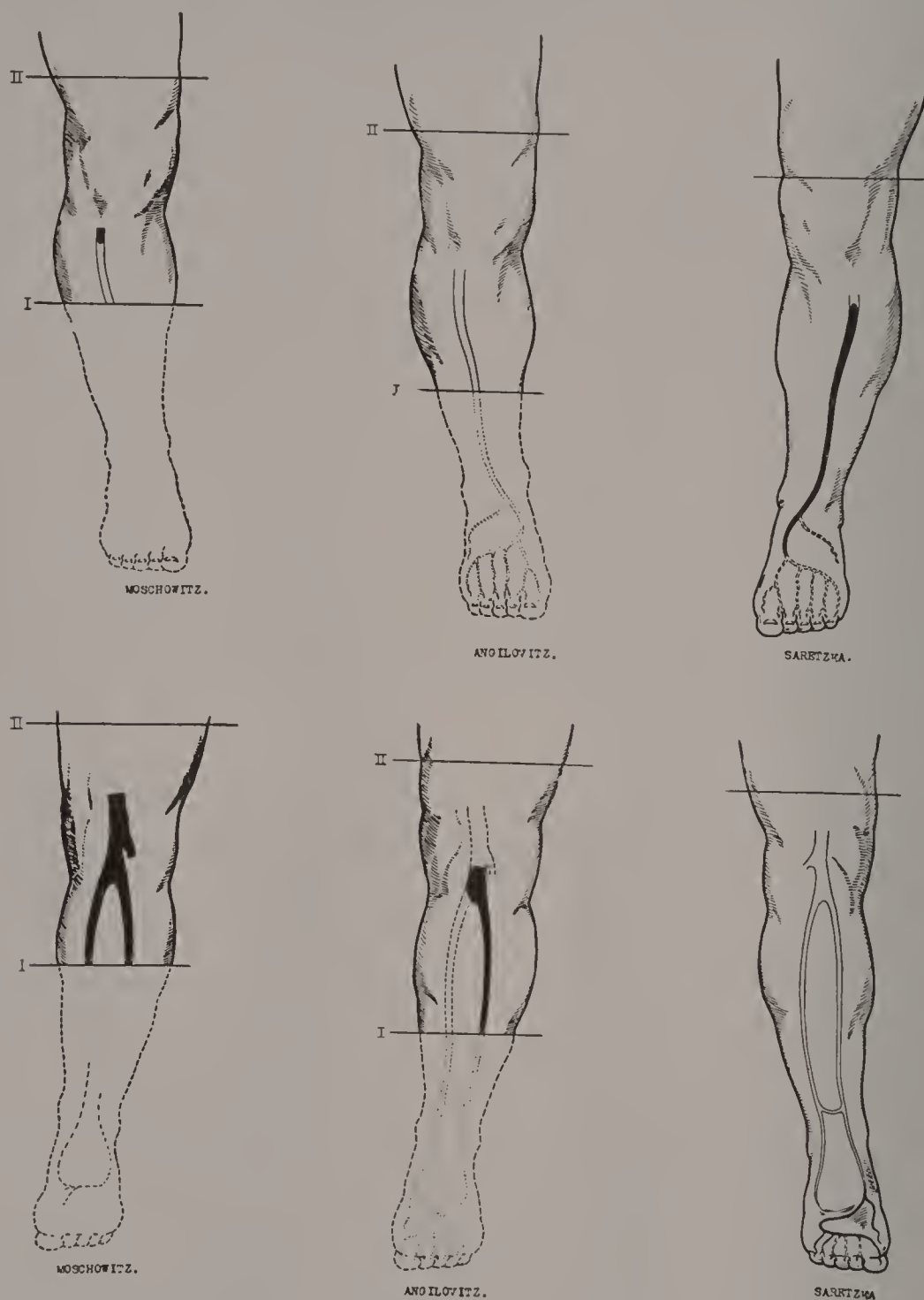


FIG. 57.—Schematic representation of extent of occlusion in thrombo-angiitis obliterans, (a, b, c from left to right).

As we trace certain of the obliterated arteries or veins upward, we are apt to meet with a change in the character of the obturating tissue. Frequently it becomes softer, more brownish in color, and terminates abruptly in the lumen of an apparently normal vessel; at other times the brownish tissue gives way to soft reddish masses which are evidently the results of recent thrombosis. In some cases this thrombotic process occupies large portions of the vessel's course; in others, it is of short extent and terminates in a long cone of recent thrombus.

The veins share equally with the arteries in the lesion of occlusion. In some cases the veins are more extensively involved than the arteries, and this is particularly true of the collaterals of the posterior tibial, which are often closed when the anterior tibial veins are open. As for the arteries, we usually find an obliteration of a part or the whole of the anterior tibial, of the dorsalis pedis, and dorsalis hallucis, an occlusion of the posterior tibial and plantar

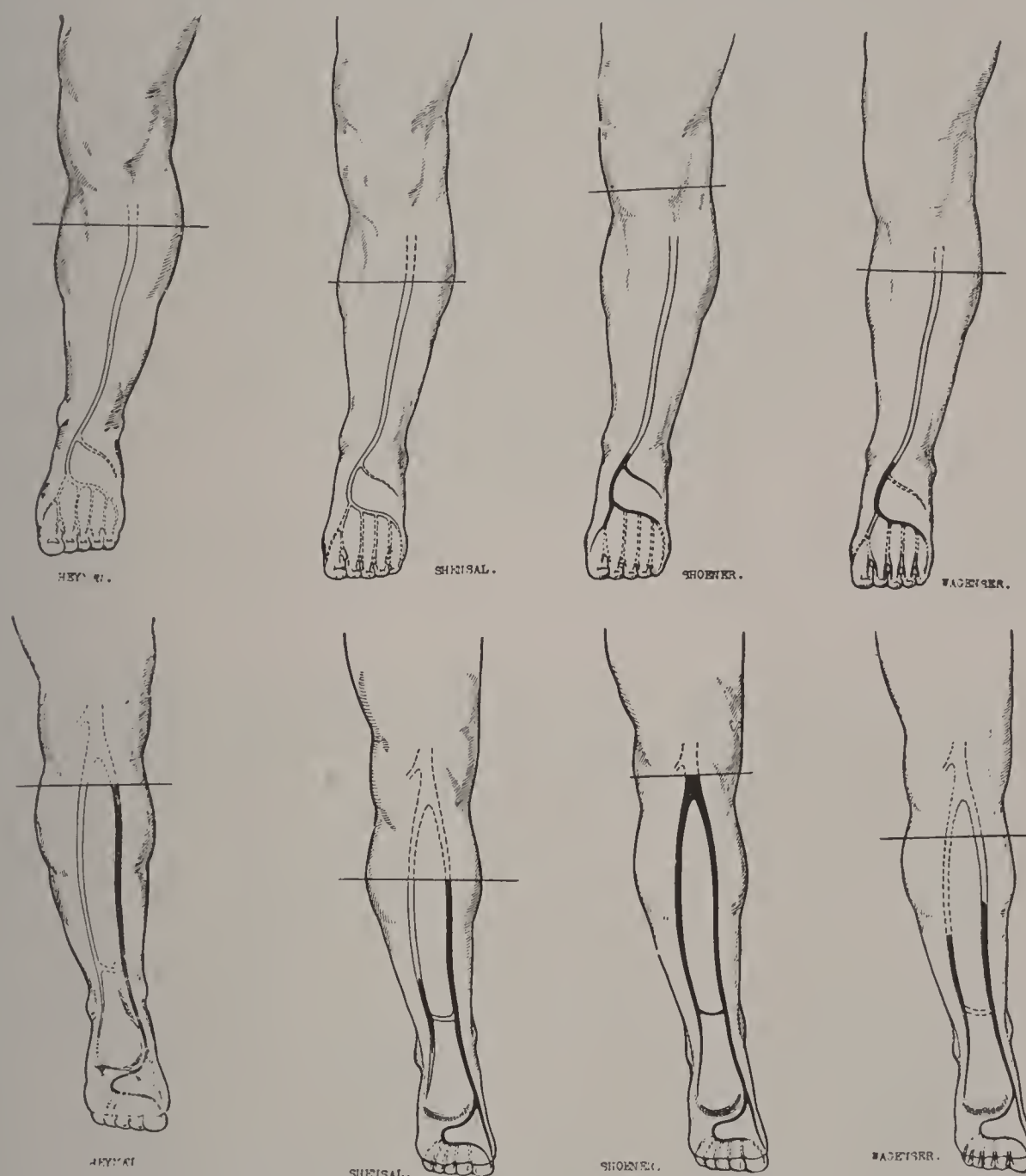


FIG. 58.—Schematic representation of extent of occlusion in thrombo-angiitis obliterans, (a, b, c, d from left to right).

vessels, with or without involvement of the peroneal. Sometimes the anterior tibial is practically normal in its upper half or upper two thirds. More rarely a large portion of the dorsalis pedis is open, with the beginning of the occlusion in the upper part of this vessel or in the lower part of the anterior tibial.

Besides the lesion of occlusion there are two other striking changes, namely, a certain amount of arteriosclerotic thickening and periarteritis. Arteriosclerosis is absent in the younger cases; when present, it is never pronounced, except in those rare instances in which the patient has suffered from the disease for many years, and has reached the age of 40 or more. As a rule,

we note but a very slight degree of whitening or thickening of the intima, here and there, in the patent portions of the vessels. In a very few cases small atheromatous patches are present.

A much more interesting and more important change is the fibrotic thickening of tissues immediately about the vessels. Wherever the vessels are occluded, there is apt to be an agglutinative process which binds together the artery and its collateral veins, and sometimes also the accompanying nerve,

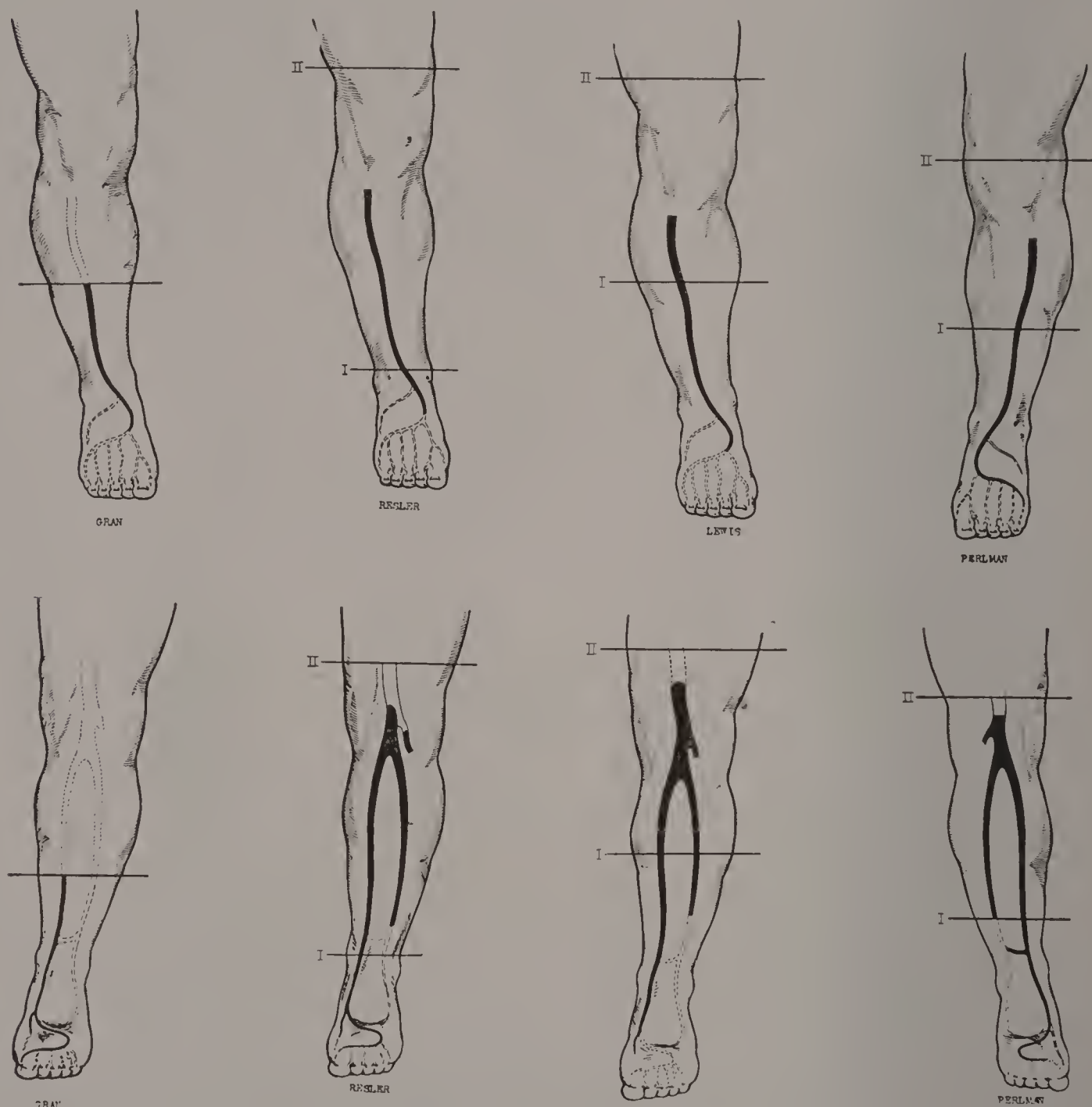


FIG. 59.—Schematic representation of extent of occlusion in thrombo-angiitis obliterans, (a, b, c, d from left to right).

so that liberation of the individual vessels by dissection is difficult. The adhesive condition is due to fibrous tissue growth, and varies considerably in its amount. The periarterial fibrosis varies, sometimes being almost absent, at other times so great, that isolation of the vessels or nerves becomes impossible, and the vascular structures make up one dense rigid cord.

Histo-pathology.—The lesions may be considered in two stages, first, the healed or organized stage, and second, the acute or incipient stage of thrombosis. Between the earliest alterations in the deep arteries and veins, and

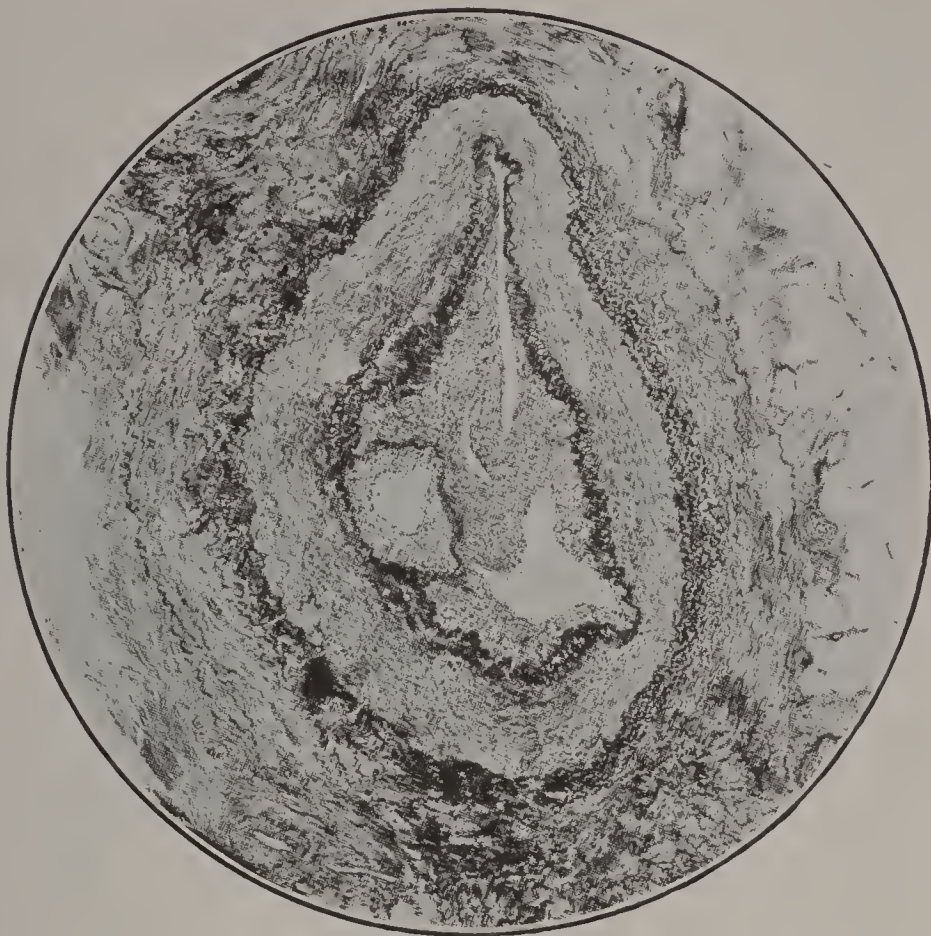


FIG. 60.—“Old” occlusion of the fenestrated or cribriform type; large canalizing vessels in fairly dense connective tissue filling the lumen of an artery.

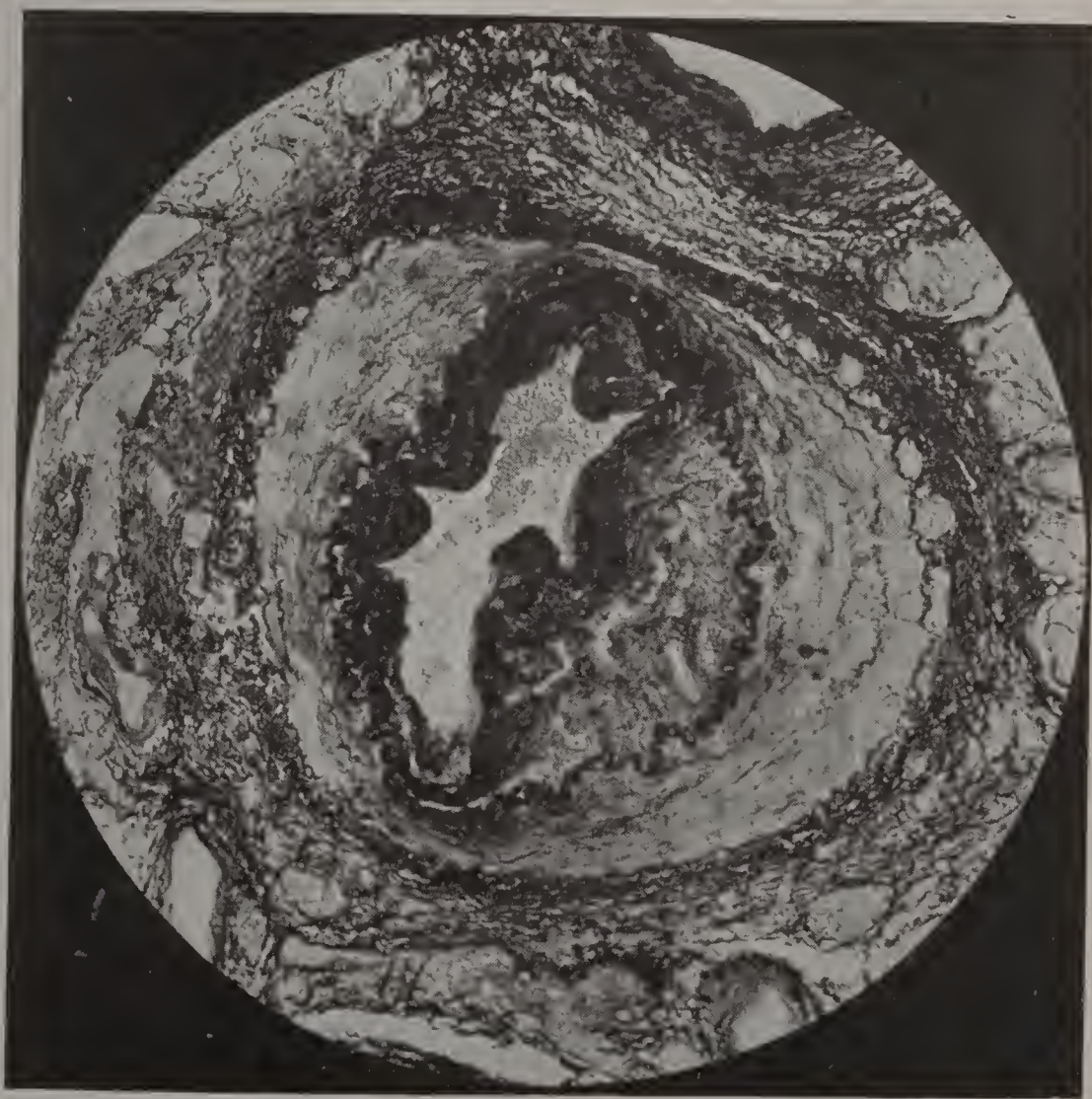


FIG. 61.—Elastic tissue formation about the canalizing vessel; a picture that can be mistaken for endarteritis obliterans.

superficial veins, and the finished product, there are a large number of intermediate pictures that illustrate the metamorphosis of the obturating clot into the intravascular cicatrix.

1. *Healed or Organized Stage.*—The most common lesion is a total obliteration of the lumina of arteries and veins by connective tissue (Fig. 60). Histologically this may be extremely varied in the general appearance, but each picture can be interpreted correctly as having its origin in the lesion of occlu-

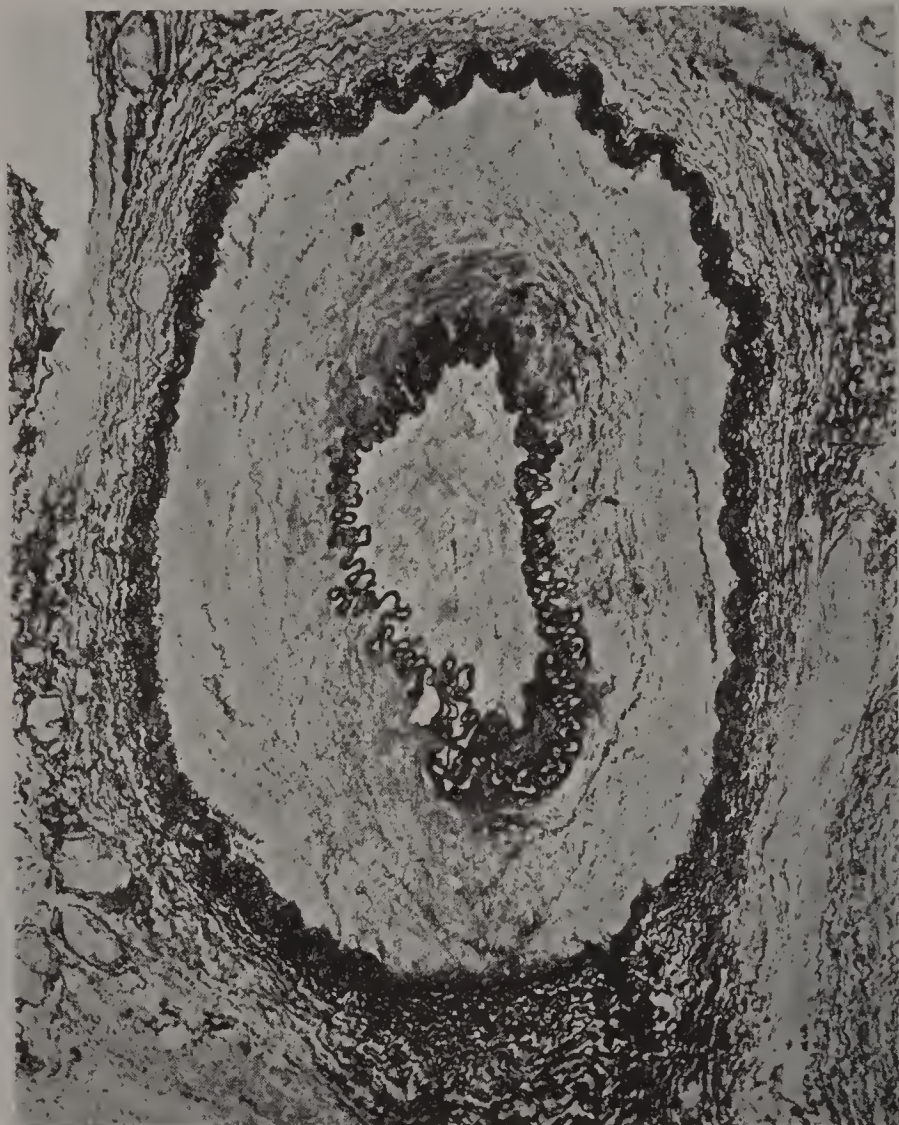


FIG. 62.—Absence of elastic tissue in thrombo-angiitis obliterans (orcein stain). The lumen is filled with old organized clot; no elastic tissue production; below, elastic tissue is in arteriosclerotic plaque.

sive thrombosis. This obturating connective tissue usually harbors numerous small vessels, pigment containing hemosiderin, and a fair amount of connective tissue cells. The canalizing vessels, when they become dilated, form smaller or larger sinuses, giving the fenestrated or cribriform lesion seen on microscopic section of the vessels, or when the canalizing vessel becomes eccentrically placed, and sufficiently large, this sinus is responsible for the appearances which have been incorrectly interpreted as the product of an endarteritis obliterans (Fig. 61).

Elastic tissue stains demonstrate characteristic differences between this process and arteriosclerosis. Thus, the region of the organized clot is almost completely free from elastic tissue (Fig. 62). The small amount which is present, is concentrically disposed about the new-formed vessels (Fig. 115). The abundant elastic tissue formation in the arteriosclerotic plaques is well seen in Fig. 63.

Still more suggestive and instructive is the finding of various stages of the disease in different members of the same vessel sheath. Thus, in Fig. 64 a large artery affords a view of the old lesion, as well as one of its venae comites. Another accompanying vein, however, is in the "acute" stage of the disease, a smaller venule or satellite being in the intermediary stage, where certain "miliary giant cell foci" make their appearance. Such pictures not only reveal the thrombotic nature of the disease, but also present an argument in favor of the following two assumptions: *that the disease begins with an inflam-*

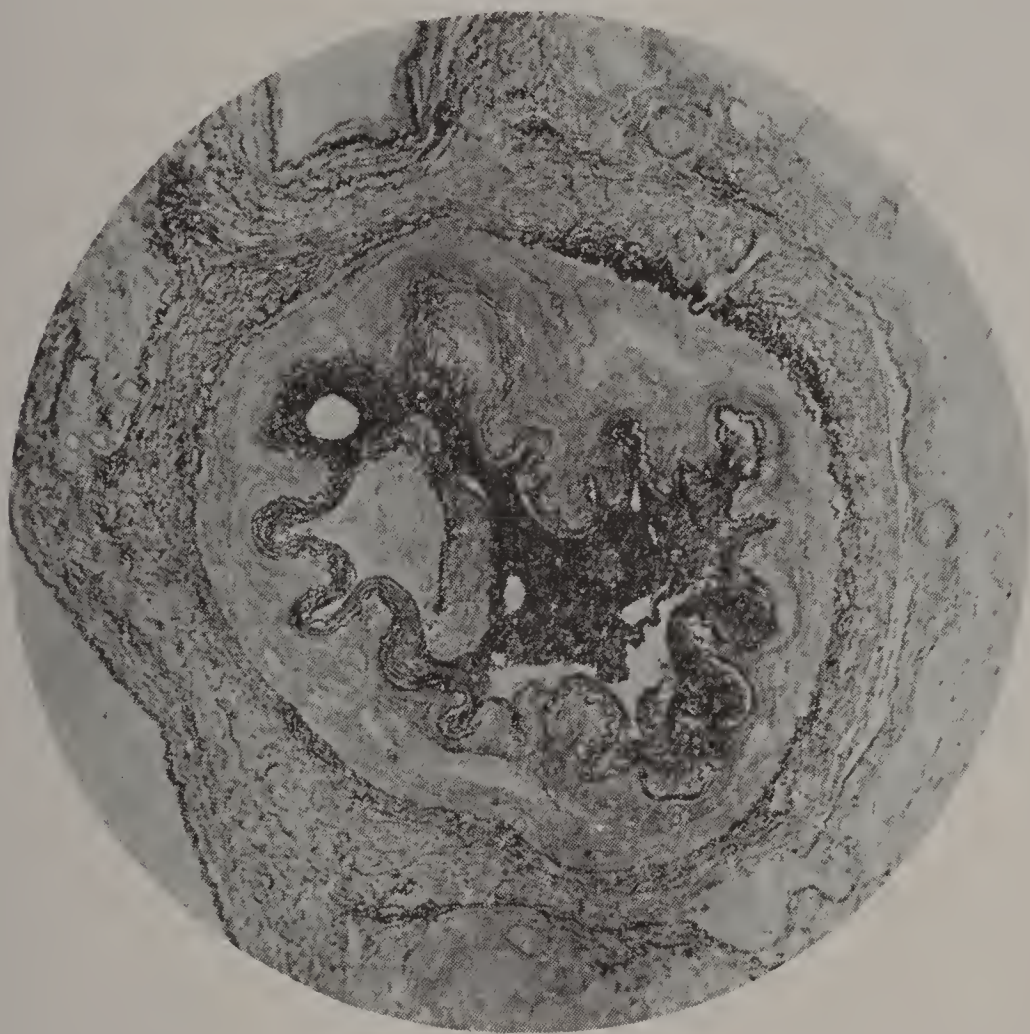


FIG. 63.—Obliterating arteriosclerotic process (orcein). The greater part of the lumen is occluded by tissue arising from the intima, and containing the typical elastic tissue found in arteriosclerosis; the small triangular clear area in the left part of the lumen contains a recent thrombus.

matory lesion attended with occlusive thrombosis, and that it affects the arteries and veins in a sort of relapsing fashion, very much in the same manner as in the veins in migrating phlebitis.

The termination of the occluding tissue in arteries and veins is often seen in the form of a rounded, convex projection looking upward (cephalad), and lying in practically healthy vessel wall (Fig. 65). At other times, the old occluding tissue is capped by an additional clot which rises in pyramidal fashion ending by a long tapering extremity.

2. *The Acute or Specific Lesion.*—The early lesions are so characteristic histologically that their appearances are practically specific for thrombo-angiitis obliterans and may permit the pathologist to make a diagnosis of the disease. They are rarely to be seen in the deep vessels, for the reason that patients do not allow amputation until the disease has lasted for months or years. However, they can be well studied when these are the seat of the

typical migrating phlebitis, and have been shown by the author to be identical with the acute lesions in the deep vessels.

The earliest changes appear to be the usual evidences of an acute inflammatory process involving all the coats of the vessel. The media, adventitia and perivascular tissues are infiltrated with polynuclear leukocytes and the

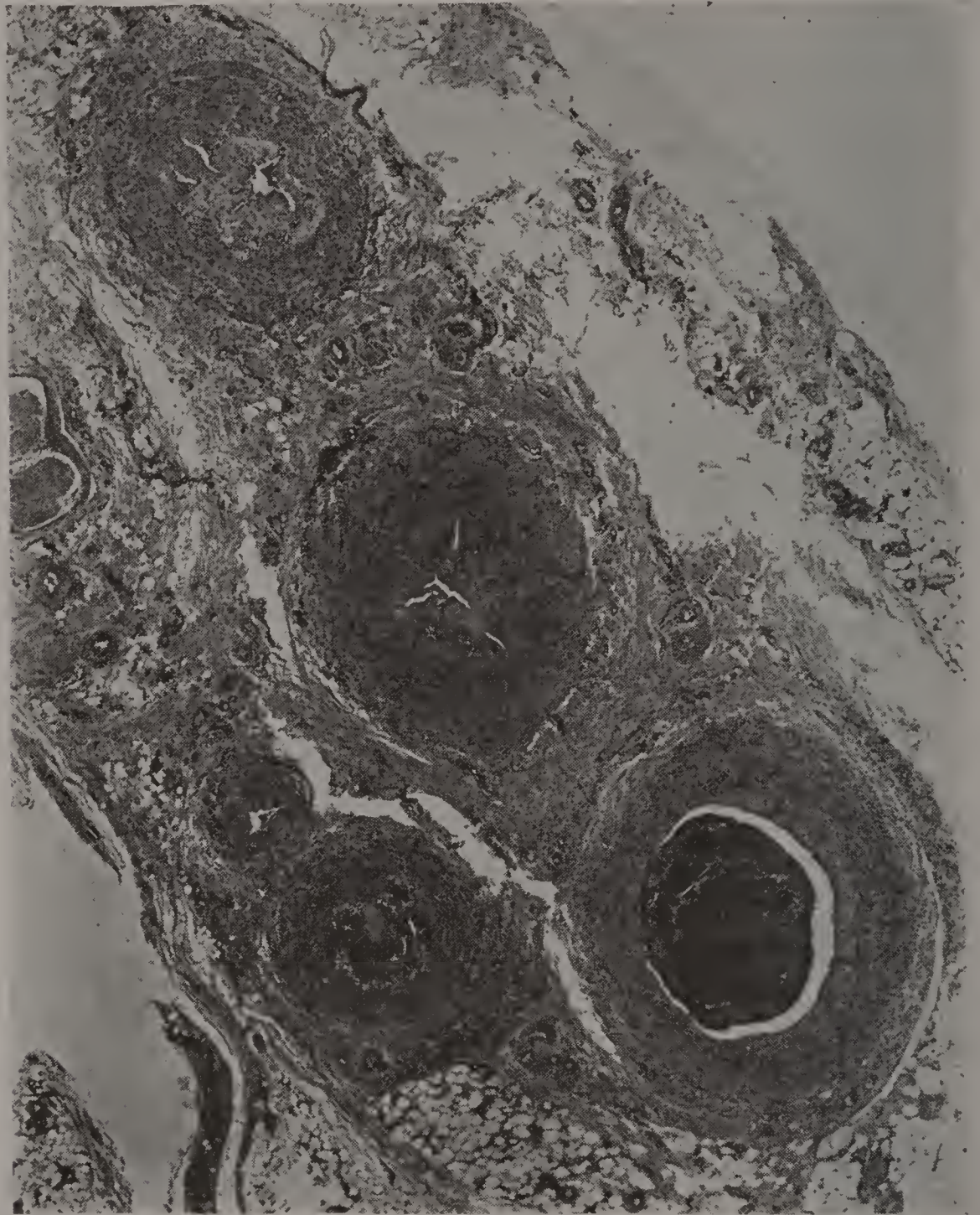


FIG. 64.—Various stages of occlusion in thrombo-angiitis obliterans; above, a vein; just below it, artery in healed fibrotic stage of occlusion; below, two veins; the larger recently occluded (acute stage) and the smaller satellite in the intermediate thrombotic stage with giant cells.

lumen of the vessel is completely filled with red clot. In the peripheral portions of the clot, larger or smaller foci of leukocytes (purulent foci) begin to form, whose growth occurs by virtue of immigration of leukocytes (Fig. 66). Certain peculiar giant cell foci develop (Fig. 67), which are characteristic. They contain giant cells, endothelioid or angioblasts and numerous broken-down leukocytes. These foci then undergo connective tissue replacement. The giant cells gradually disappear, numerous small vessels are formed, the

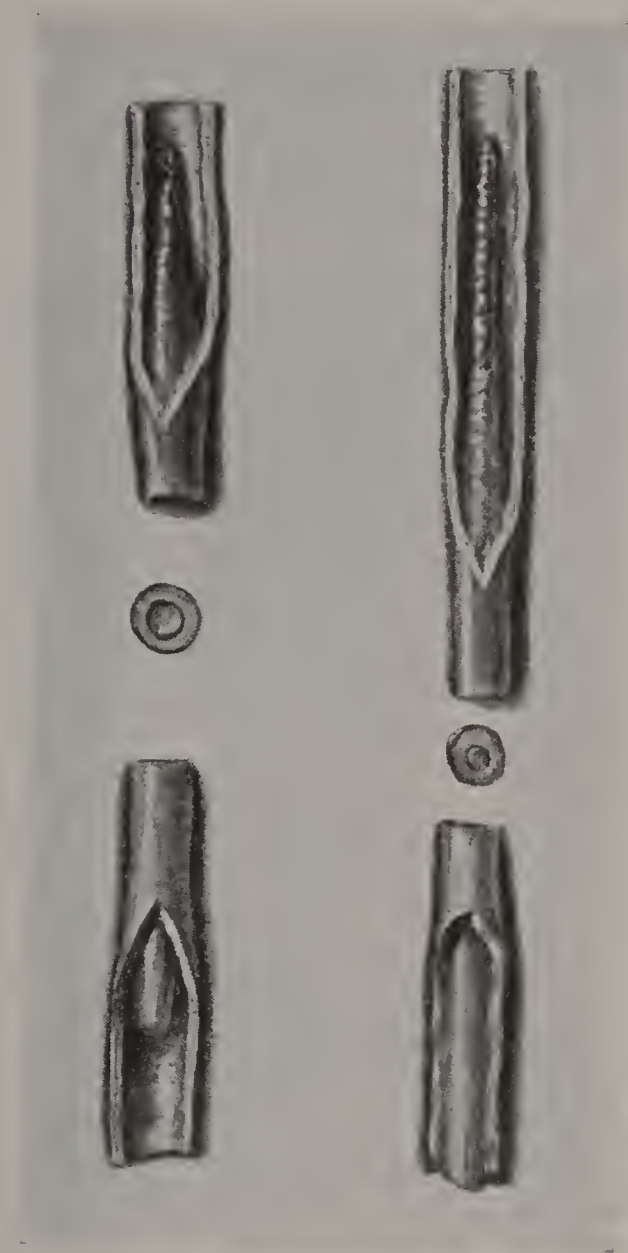


FIG. 65.—Thrombi in apparently healthy vessels. Upper figure: Conical type of clot, there being an accretion or stagnation red clot, over the old obturating organized clot. Lower figure: Rounded extremity of the older type of clot ending in apparently healthy vessels.



FIG. 66.—Acute lesion in internal saphenous vein; on the right, purulent focus; on the left remaining crescentic portion of lumen filled with organizing clot. (Giemsa stain.)

final product being a fibrous nodule containing vessels and some pigment. In the rest of the occluding clot, the organizing process is somewhat different, resembling that which characterizes the organization of blood clot in other thromboses.



FIG. 67.—High power appearance of characteristic "miliary giant cell" focus in thrombo-angiitis obliterans.

In short, the lesions in thrombo-angiitis obliterans are in chronological order, an acute inflammatory lesion with occlusive thrombosis, the formation of miliary giant cell foci, the stage of organization or healing, with the disappearance of the miliary giant cell foci, the organization and canalization of the clot, the disappearance of the inflammatory products, and the development of fibrotic tissue in the adventitia that binds together the artery, vein and nerves.

CHAPTER LXII

THROMBO-ANGIITIS OBLITERANS—MORE DETAILED HISTO-PATHOLOGY

For the student of pathology, a more comprehensive account than is needful for the clinician may be of value. More detailed knowledge carries with it the foundation for a correct interpretation of other occlusive arterial lesions. We have only dwelt upon the essential alterations in the previous chapter. Here, we shall discuss at greater length, (1) the acute lesions in the superficial veins; (2) the acute lesions in the deep vessels; (3) the intermediary stages of organization, and (4) cicatrical, "healed," or completely organized stage.

The Acute Stage of the Disease.—In superficial veins it has already been pointed out that the superficial, that is, the cutaneous and subcutaneous



FIG. 68.—Infiltration of the media (below) in a vein and migration of leukocytes into the purulent focus (above).

veins, offered the best material for the study of the earliest or acute lesions of thrombo-angiitis. The site of predilection for this thrombophlebitis seems to be somewhere in the lower half of the territory of the internal saphenous vein, although the external saphenous, saphenous of the thigh, median basilic, median cephalic veins of the forearm and foot may also be

attacked. Clinically two types of affection manifest themselves, either as indurated strands or cords one-half to two, three, or four inches in length or as small nodosities. Both of these are the expression of an acute thrombophlebitis, with marked perivascular inflammatory infiltration; in the first case, in and about larger veins, in the second, involving minute venules or cutaneous tributaries.

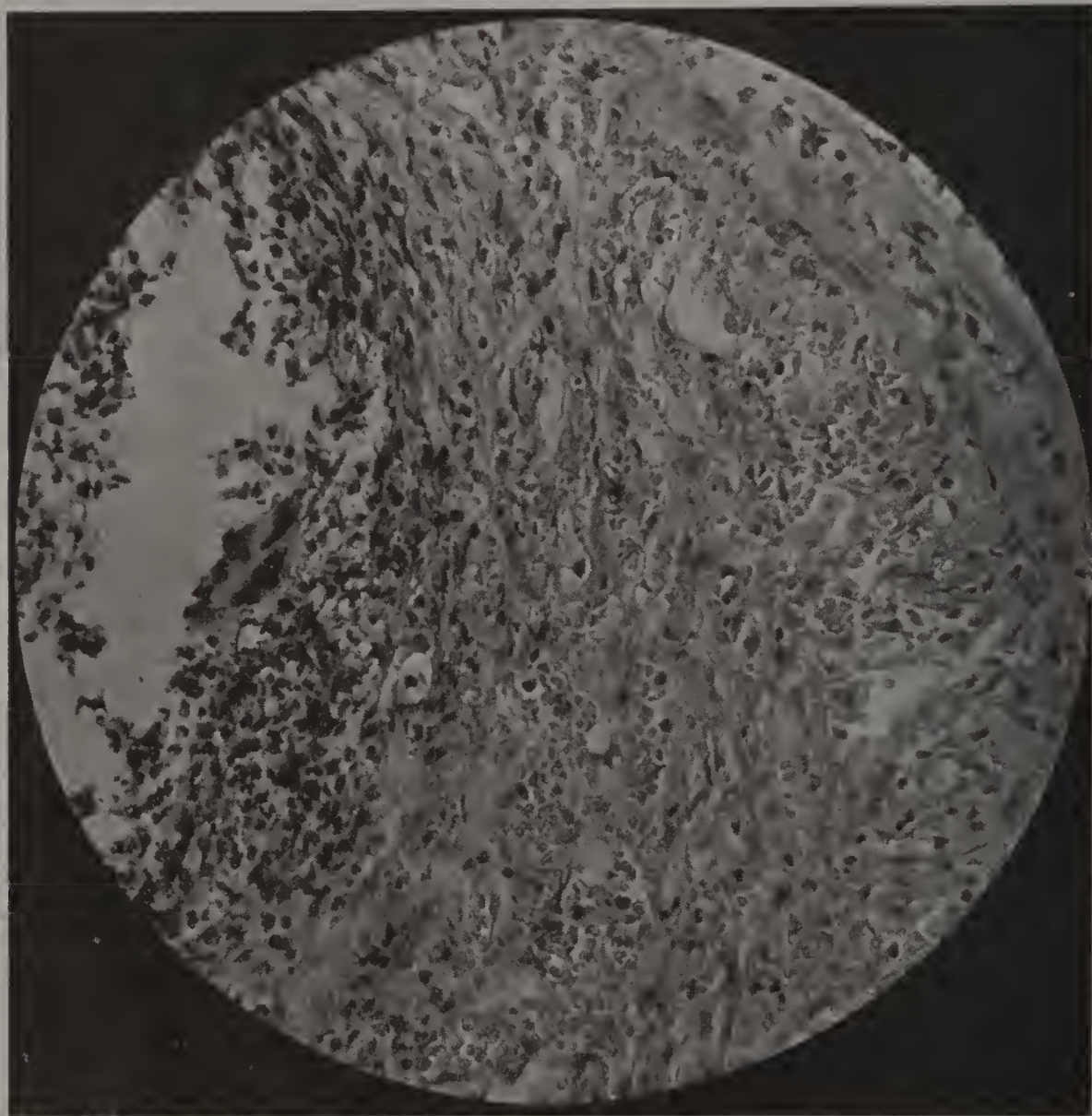


FIG. 69.—Normal organization of red clot on the right, the periphery of a purulent focus on the left. In the former new capillary growth, in the latter compressed concentric layers of angioblasts (endothelioid), and giant cell formation.

Even in the cases of migrating phlebitis it is not an easy matter to procure material in the proper stage of the disease. It is seldom that the patient will consult us at the very onset of the phlebitis, and it is even rarer to be able to acquire the veins by extirpation at this time. And that is why many of our biopsies were disappointing, yielding lesions already in the stage of healing and connective tissue organization. On the other hand, these difficulties were of advantage in that we were enabled to obtain veins showing many stages of the process and could then synthesize the individual findings into a composite picture of the evolution of the disease.

The general impression obtained from a cursory examination of many sections of the affected veins is that we are dealing with an acute inflammation of the vessel wall, invasion of the media with polynuclear leucocytes, marked reaction on the part of the adventitia, and perivascular connective tissue,

and an obturating thrombosis, which practically always leads to complete closure of the lumen. In the clot which is for the most part red, but also contains platelet areas and fibrin, there appear either the typical "miliary giant cell" areas, or the precursors of these, collections of polynuclear leucocytes arranged in veritable miliary abscesses.

For an elucidation of the nature of the pathological process and of its metamorphosis into the stages just preceding the healed connective tissue product, it may be best to refer to photomicrographs selected from many hundreds of sections. In these we will attempt to show that an inflammatory

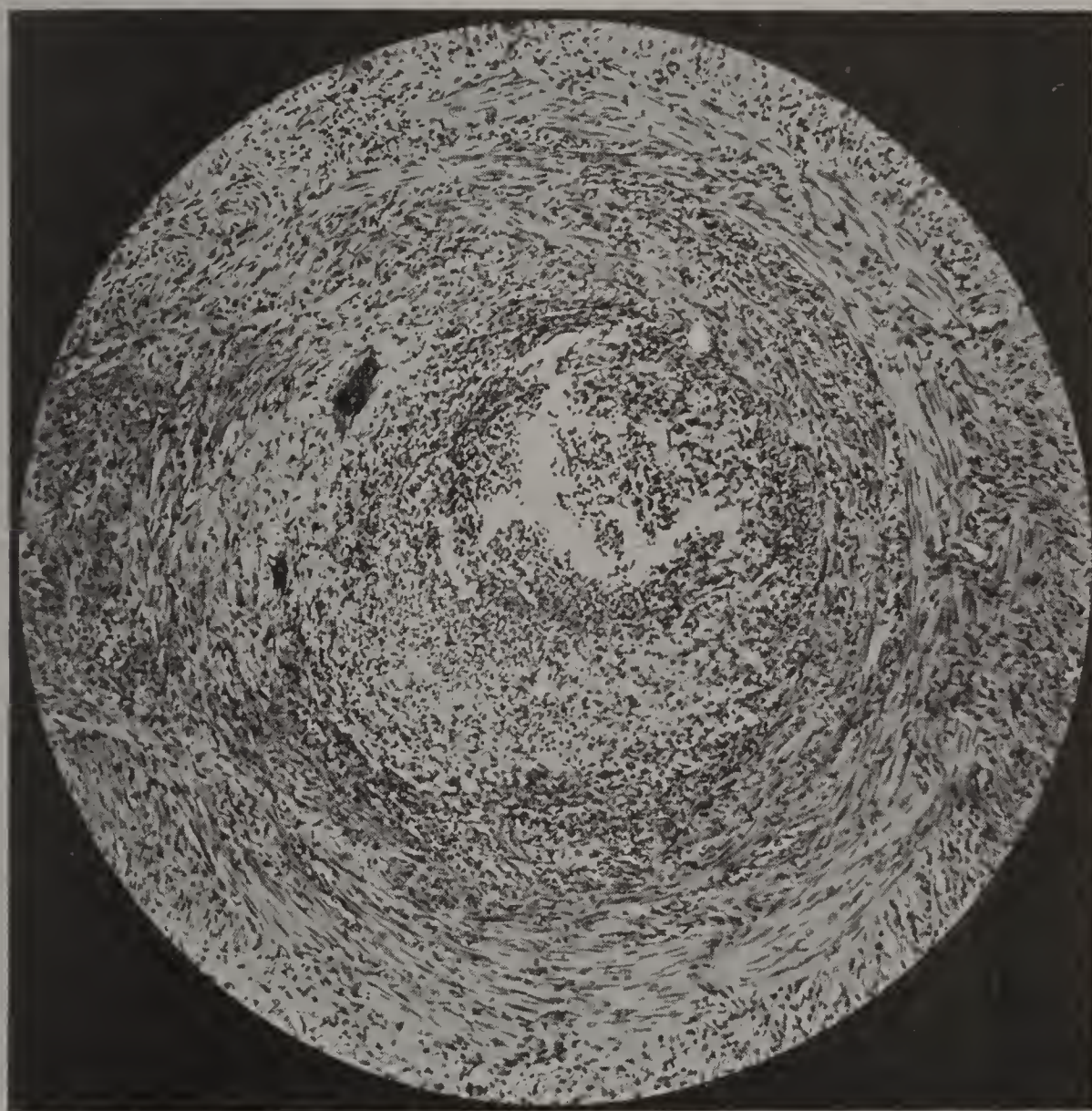


FIG. 70.—Greater magnification of Fig. 72; at 2 o'clock the miliary focus; the giant cells at 9 and 10 o'clock.

phlebitis and periphlebitis (or arteritis and periarteritis) are the initial lesions, synchronous with the phenomenon of complete vascular occlusion by clot; that in the proper evolution of this disease, healing is the rule, in so far as the products of the inflammatory stage disappear, and give way to fibrous tissue; that in the course of this healing, certain characteristic pictures are evolved—such as the miliary giant cell foci—whose *raison d'être* can easily be explained; and, finally, that the peculiar architecture of the anatomical framework, its specificity for thrombo-angiitis, and its purulent foci, all favor the assumption that some specific agent, parasitic or bacterial, is responsible for the disease.

Of all the pictures, that depicted in Fig. 66 and taken from a portion of the saphenous vein is the most instructive, for it bears testimony to the presence

of an inflammatory lesion. Here we see a vessel filled with clot, a portion of it undergoing organization in the normal fashion, the rest occupied by a focus of polynuclear leucocytes. Were it not for the rapid changes in the clot, such findings would doubtless have been more frequent amongst the many vessels examined. But it takes only a very short time for the process of organization to completely metamorphose these purulent areas, and develop the more usual pictures containing miliary giant cell foci.

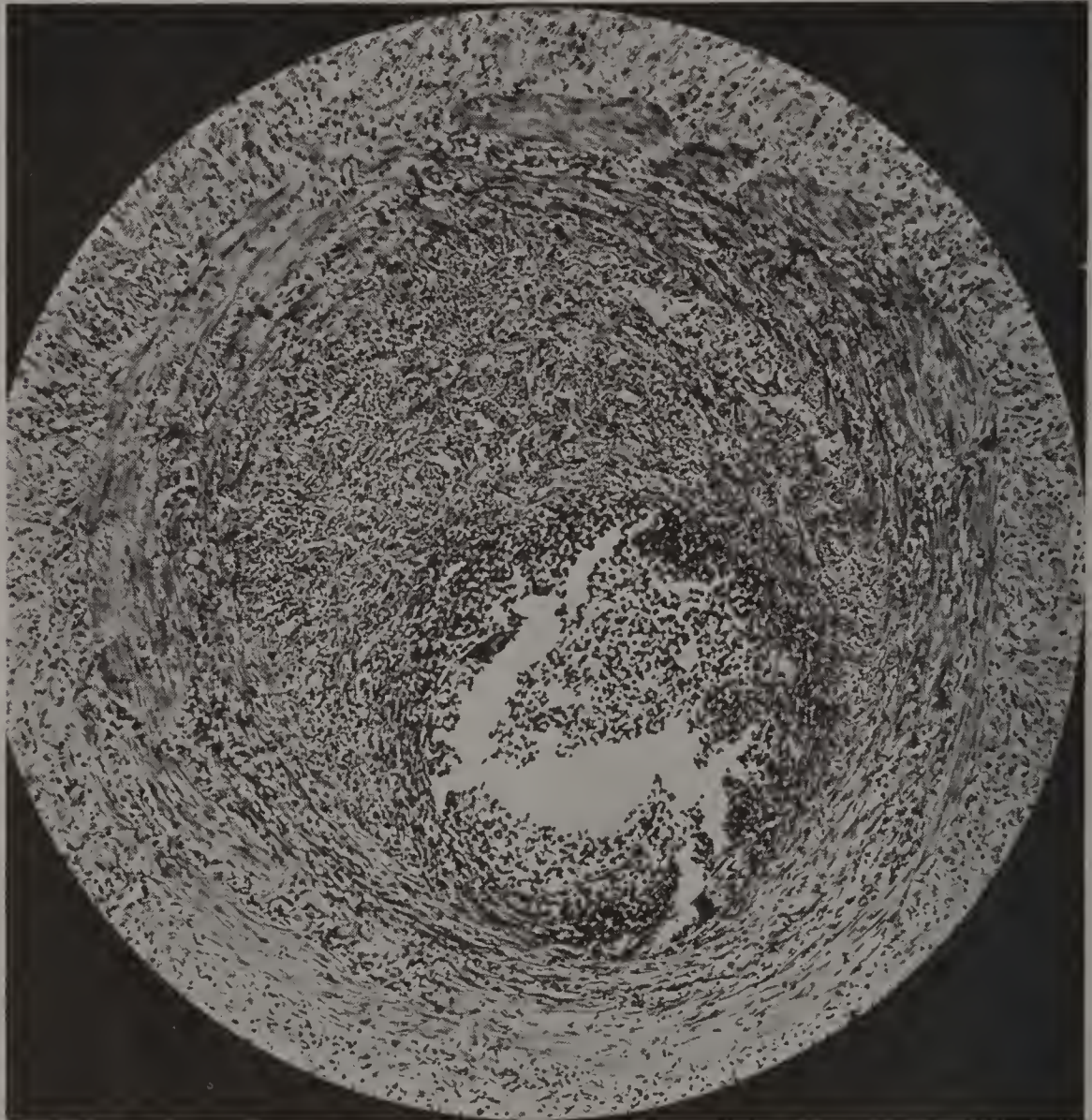


FIG. 71.—Acute stage in superficial vein; at 5 o'clock miliary abscess; rest of lumen filled with red clot, in process of "bland" or normal type of organization.

Such aggregations of cells are not due to fortuitous grouping of the white blood corpuscles, for they not only contain more leukocytes than could have issued from the intravascular blood stream, but can be seen to owe their existence to immigration of cells by way of the media (Fig. 68). Elsewhere, the lumen may be occupied by red clot, in which the typical normal process of organization is going on *pari passu* with certain atypical changes in the pus focus (Fig. 69), alterations that lead to the production of the specific pictures previously described.

In the media as well as in the adventitia the evidences of inflammation are manifested by intense infiltration with leukocytes (Figs. 68, 70 and 71), which seems to be more marked in the superficial (subcutaneous and cutaneous veins), than in the deep vessels. Then the fixed cells multiply. Later the cellular elements diminish in number, and even disappear, being replaced in the media by new vessels, in the adventitia by new formed fibrous tissue.

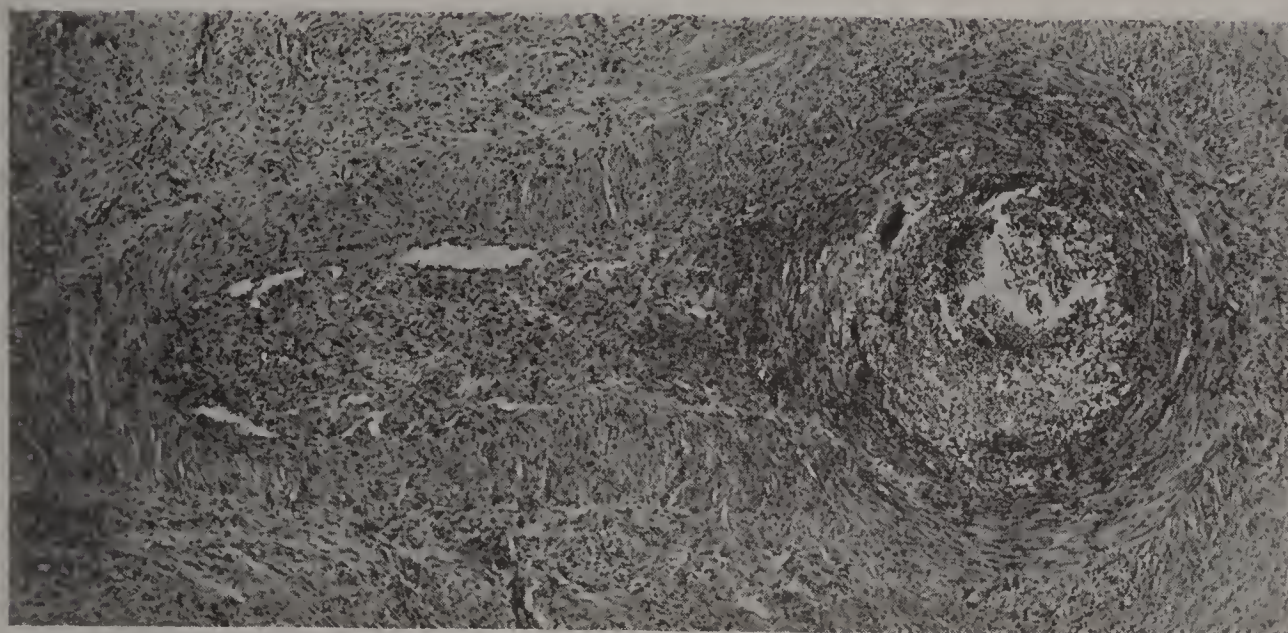


FIG. 72.—Acute lesion in vein; on the right, the vein is seen in cross section; on the left, a tributary is cut longitudinally and shows an older process.

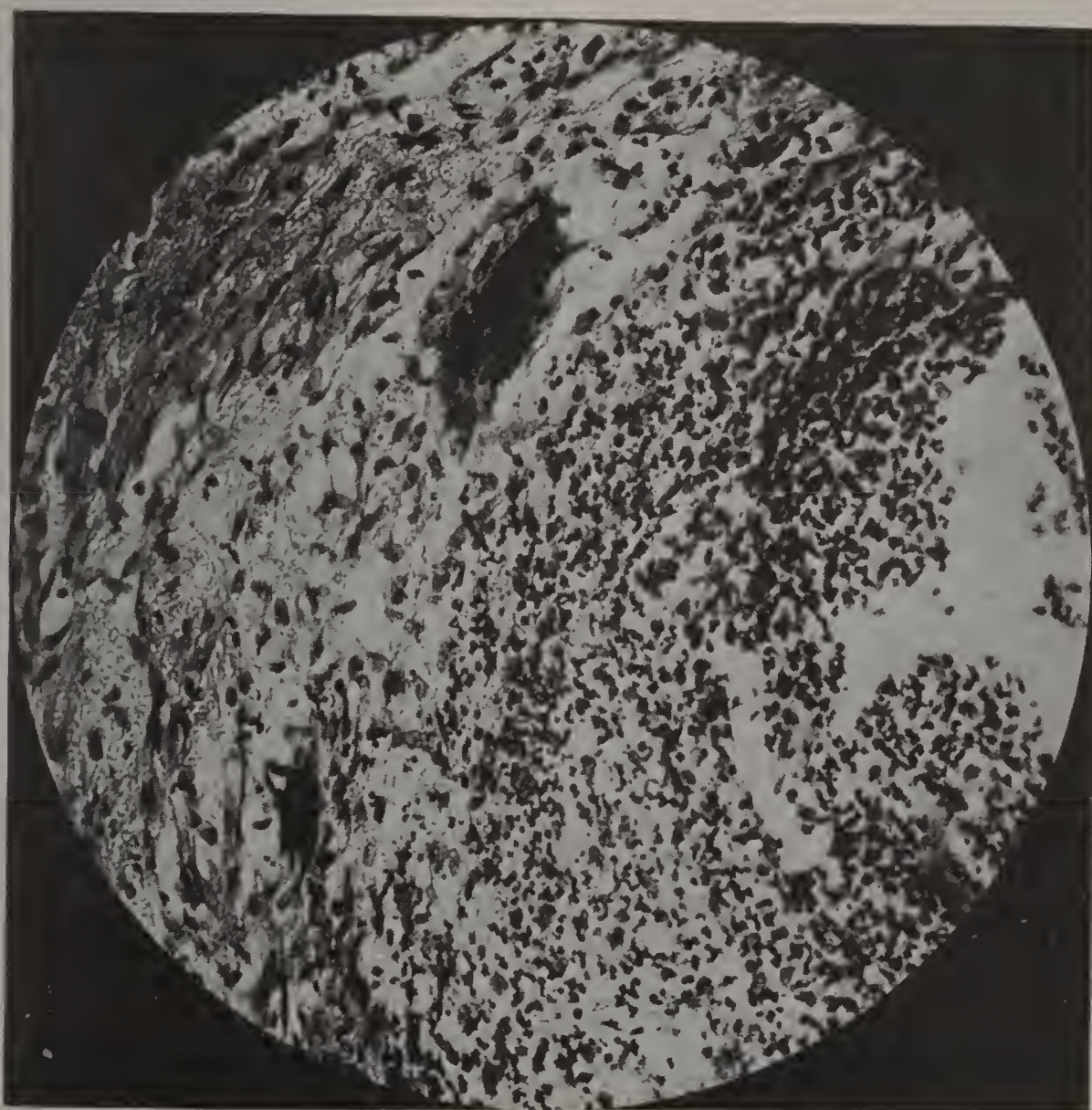


FIG. 73.—High power of Fig. 70; the margin of the inflammatory focus is seen on the right; the bland type of organization on the left with the giant cells at the margin.

In Fig. 72 there is a beautiful example of a vein with the acute lesions. Section has been so made that the vessel (on the right) is cut transversely, and on the left either strikes the same longitudinally as it makes a sharp bend, or possibly goes through a large tributary. The purulent focus is well depicted (at 2 o'clock) on the right, with the giant cells clearly defined. Where the section passes in a more longitudinal direction and partly tangentially through the media, it reveals much older obturating tissue in a solid organized form, the inflammatory process in the wall of the vein having disappeared.

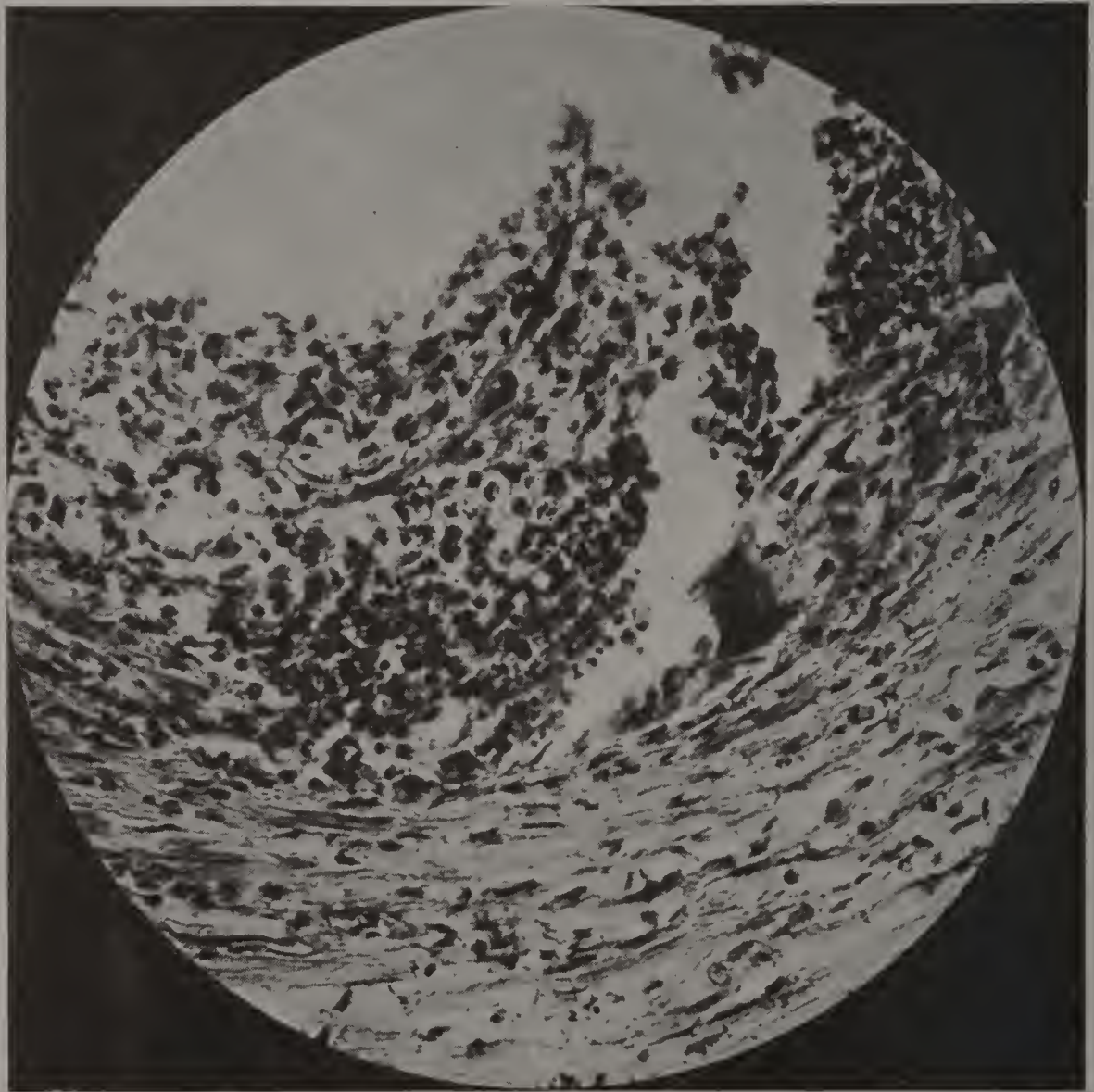


FIG. 74.—High power of a portion of Fig. 71; acute stage illustrating giant cell development, and aberrant ingrowth of angioblasts.

The same vessel seen at another level and reproduced in Fig. 70 will clearly illustrate some of the finer details of these distinctive inflammatory responses. To the left where the clot is in part of bland variety (red portion) organizing capillaries can be seen. The intense cellular infiltration of all of the coats of the vein and especially the inner layers of the media is made apparent. The margin of a miliary purulent focus, the giant cells and the adjacent area of "bland"¹ organization are brought better to view in the high power photograph reproduced in Fig. 73.

Returning to a consideration of the occluding tissue, the two different portions merit separate discussion. In the red portion of the clot we see an

¹ Refers to normal and non-specific type of organization.

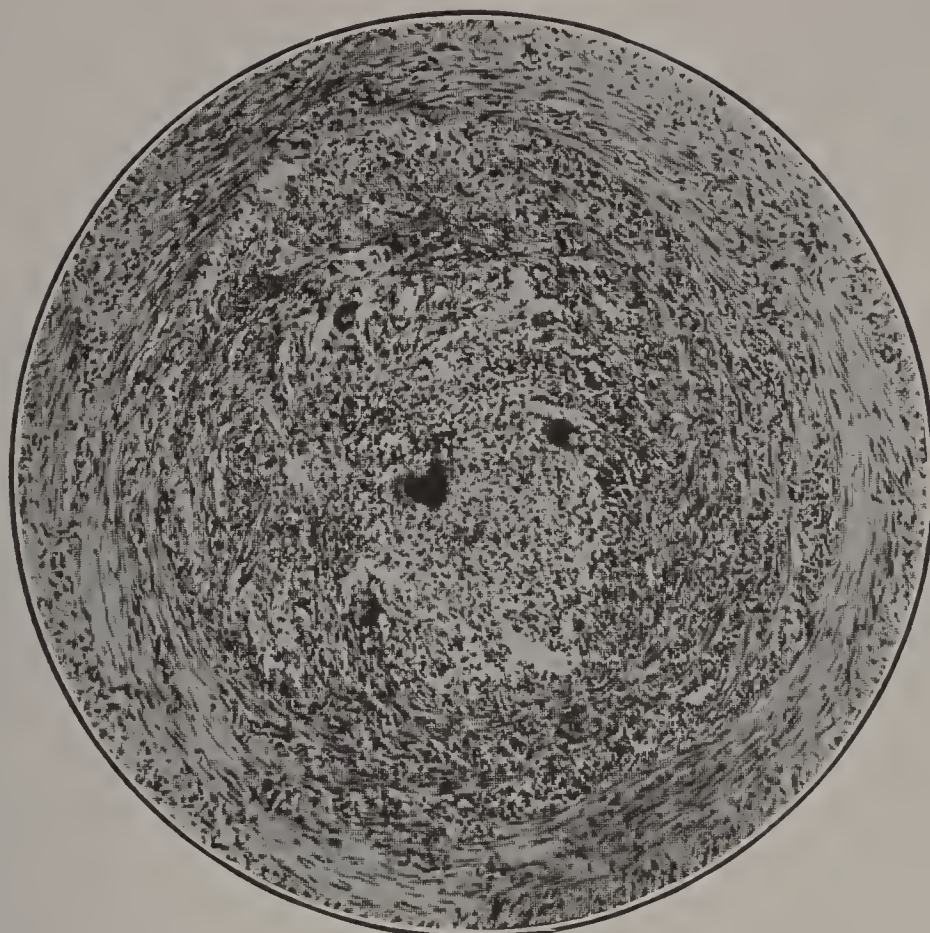


FIG. 75.—Acute lesion in superficial vein; media infiltrated; giant cell focus.

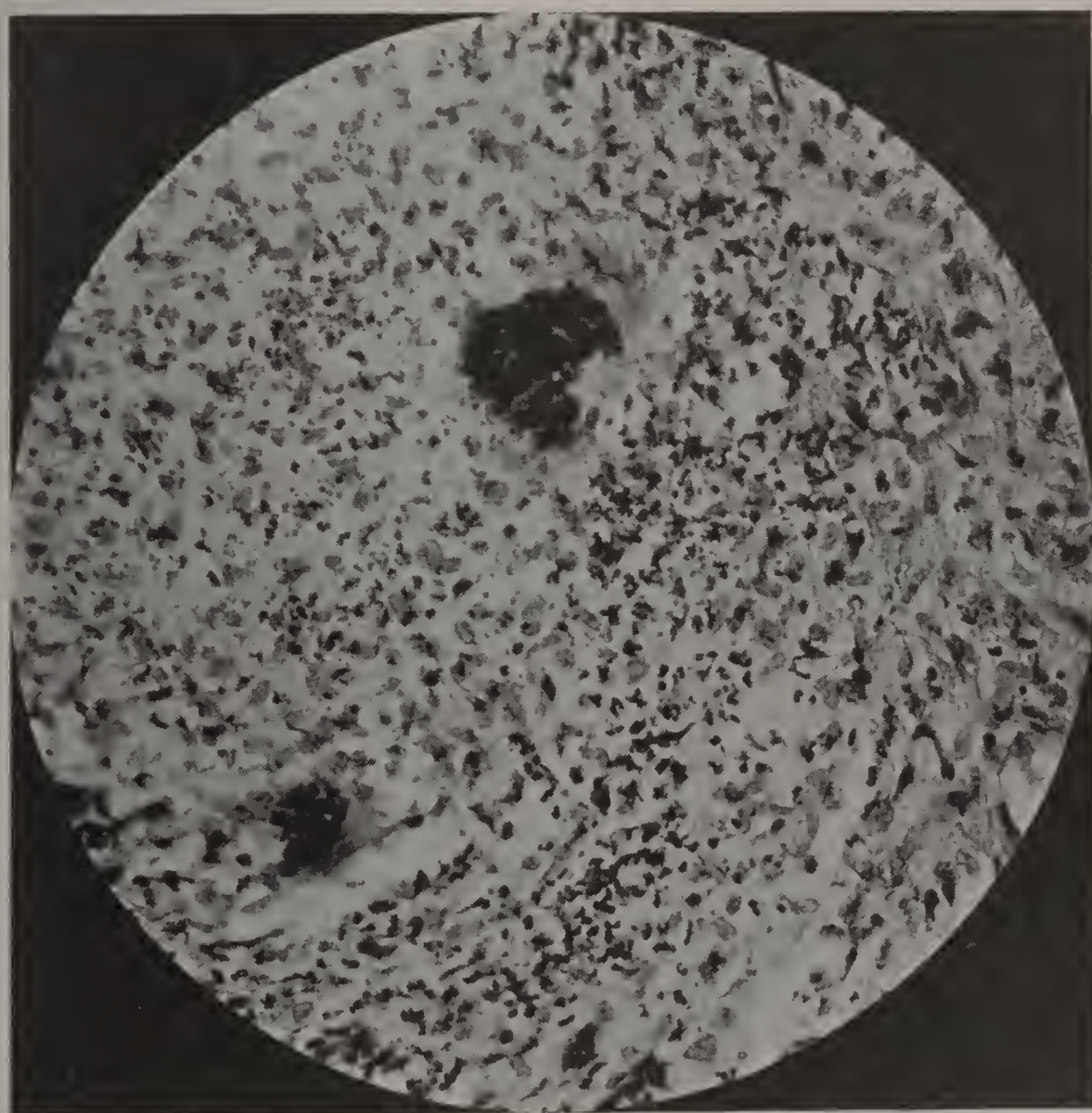


FIG. 76.—High power of Fig. 75; purulent focus with large giant cells; breaking down of leukocytes illustrated.

orderly penetration of capillary sprouts, the angioblasts forming new capillaries (Fig. 69), just as occurs elsewhere in the organization of thrombi, in thrombosis of arteriosclerotic vessels, in the accretion clots capping the "specific" clots of thrombo-angiitis, or in any clot in which suppuration is absent. These areas of organization may occupy a crescentic portion of the lumen (Fig. 71) when there is a single purulent focus, or may constitute various parts of the clot if several miliary abscesses are present.

If we carefully study the transition of these typically organized zones into the purulent foci, we shall learn why and how the giant cells are formed, and will be able to explain the development of the later stages of the pus foci

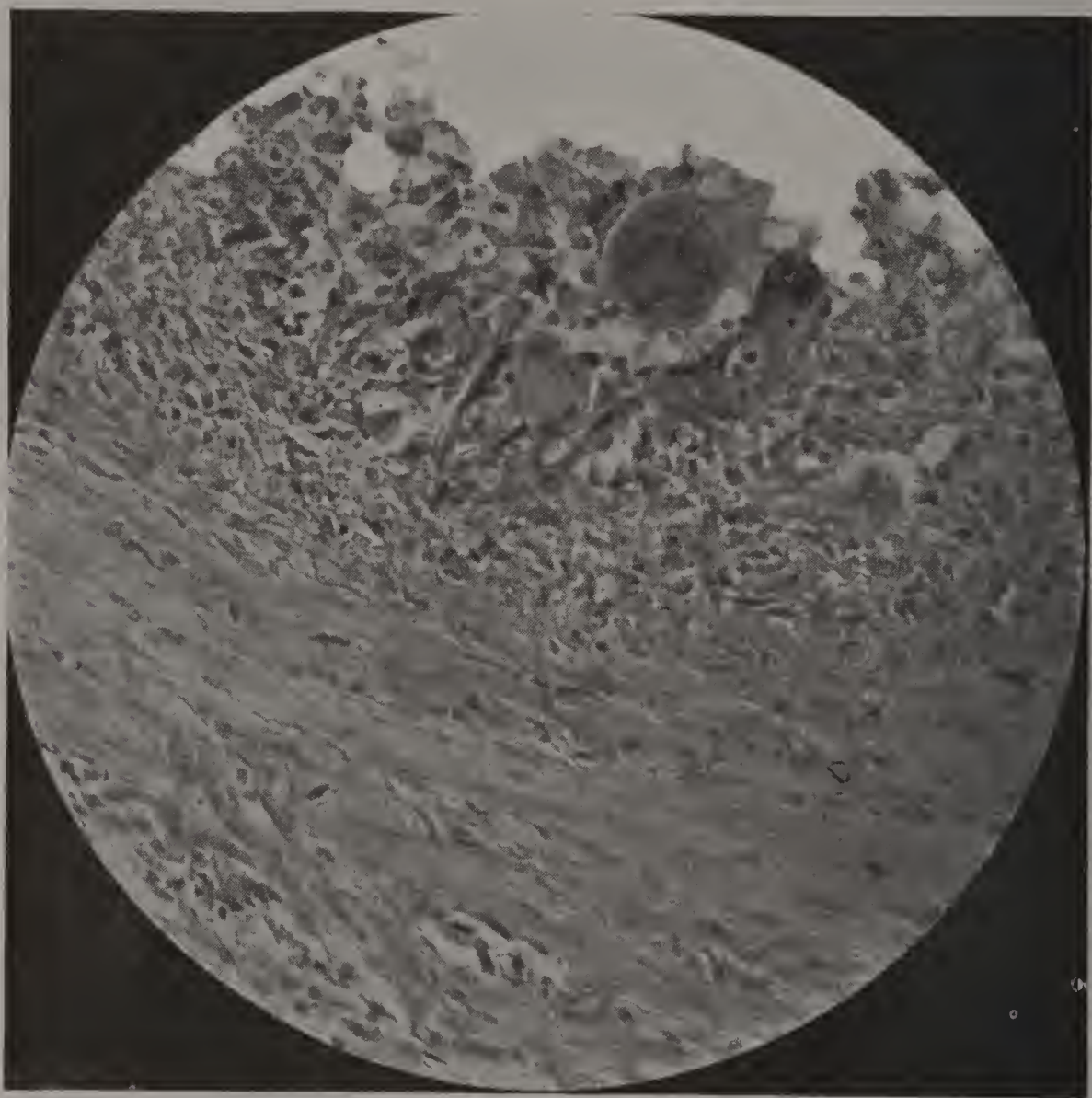


FIG. 77.—Giant cell formation in thrombus filling posterior tibial artery, angioblasts directly traceable into these cells.

—the miliary giant cell foci. As the angioblasts approach a purulent focus, the cells arrange themselves in compressed, concentrically disposed layers (Fig. 74), penetrate the pus foci in a wayward fashion, or form giant cells, never showing a tendency to orderly invasion, nor any ability to form vascular sprouts (Figs. 71 and 74). The giant cells must be regarded as abortive attempts on the part of the angioblasts to produce new vessels.

A scrutiny of Fig. 74 will demonstrate how the angioblasts became impotent, as it were, at the periphery of purulent focus, some cells becoming merely distorted and unable to enter the leukocytic area at all, others passing in for a short distance, or proliferating *in loco* into a giant cell.

Figures 75 and 76 illustrate the same phenomena, the giant cell formation at the periphery of the infectious focus; and in the high power picture (Fig. 73) there is clearly indicated the contrast between normal purposeful vessel formation in the red clot and the bizarre formation at the edge of and in the purulent focus. In Fig. 77, taken from a posterior tibial artery, the abortive growth of angioblasts is also illustrated.

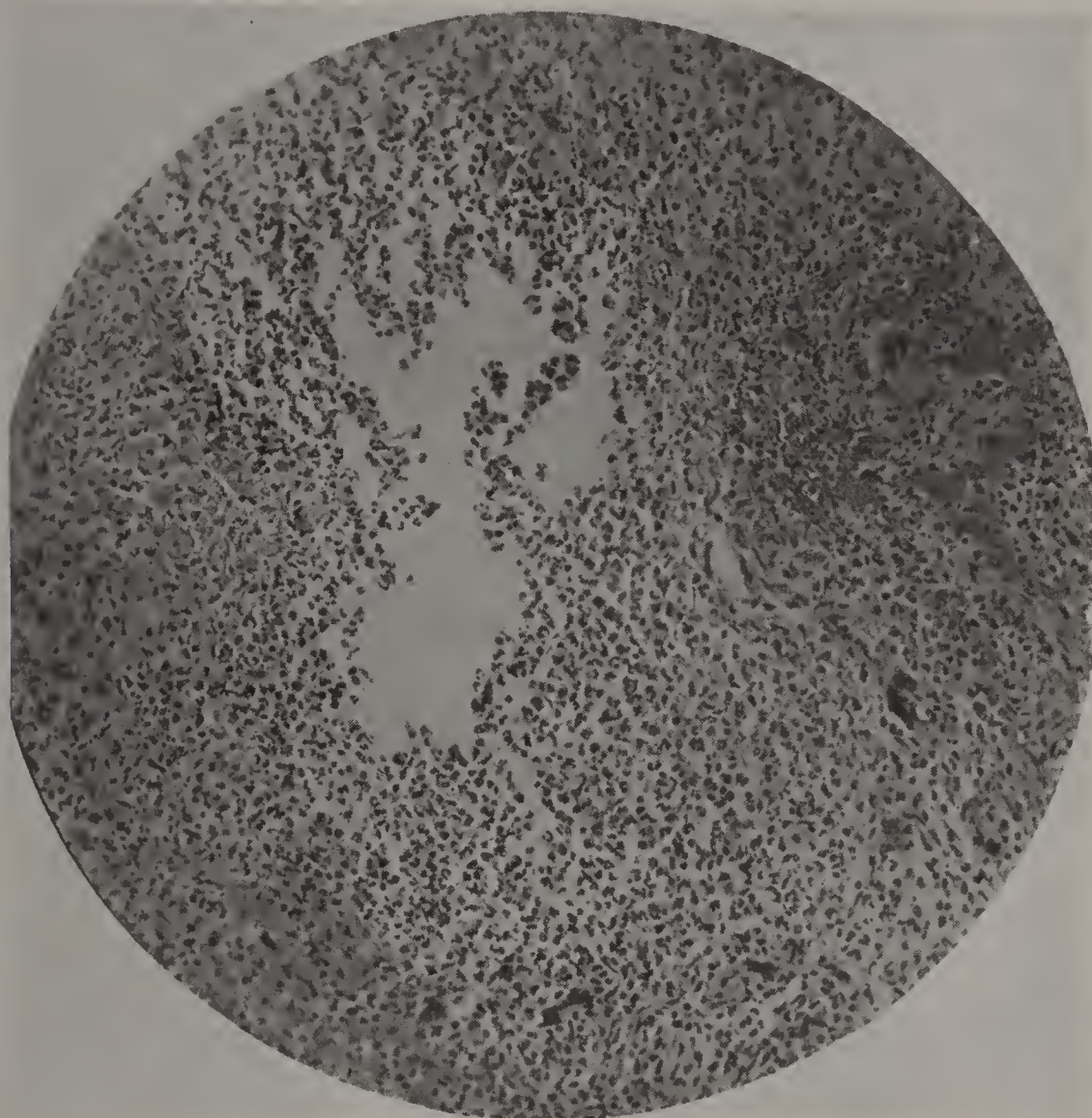


FIG. 78.—Acute lesion taken from the clot of a vein; the greater portion of the area is occupied by polynuclear leukocytes; about the periphery of the purulent focus there are numerous giant cells.

Even more striking than in the last sections is the demonstration of these facts in Figs. 71 and 74, where a vein in the “acute” stage also contains a normally organized crescentic zone and one large miliary abscess. The angioblasts can here also be discerned passing into and forming giant cells and wandering in irregular, erring fashion amongst the leukocytes.

The muscle fibers are usually widely separated by the invading cellular elements, which are for the most part polynuclear and endothelial leukocytes. But where the process has existed for a long time, a large number of new formed capillaries still further increase the tissues that separate the muscle fibers. These vessels can be traced into the adventitia, which is also considerably increased in thickness, and the fatty tissue in the immediate neighborhood, as in the older specimens, has become more dense and replaced by connective tissue. Even the adjacent nerve fibers show thickening of their perineural connective tissue and are surrounded by mononuclear leukocytes in collections of varying size.

To pass in review all the kaleidoscopic appearances that mark the transition of these characteristic foci into the final, healed connective tissue product would be a work of supererogation, for the selected photomicrographs now to be shown will suffice to make our argument clear. Unable, then, to organize the pus foci, the angioblasts proliferate at the periphery of these. As the leukocytes disintegrate (Figs. 76, 78, 79 and 80) and the toxic products are absorbed, the atypical distorted angioblasts—now looking like typical “endothelioid” cells—together with the giant cells, gradually replace the

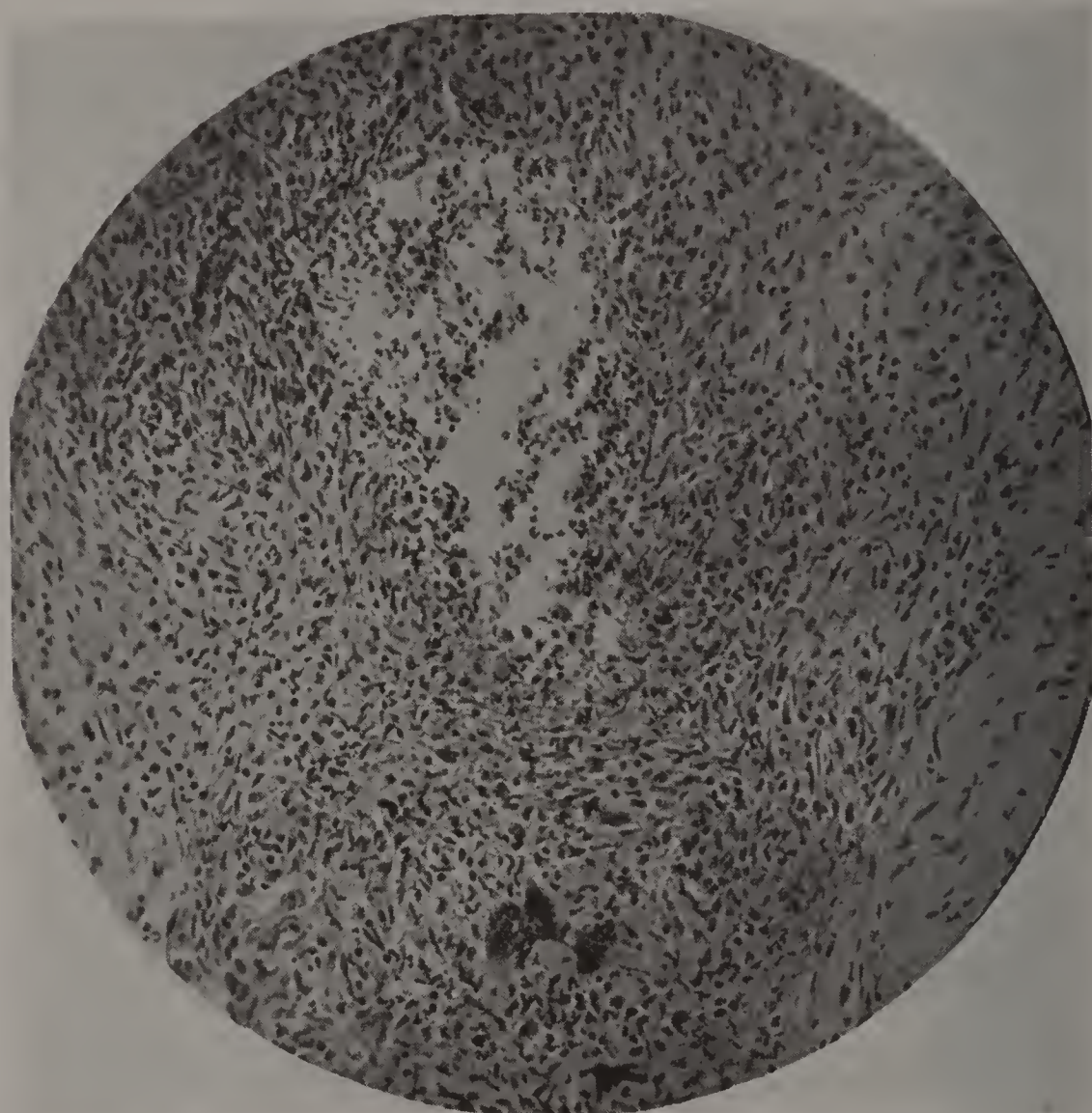


FIG. 79.—Acute lesions; miliary focus in which the process of organization is quite advanced, the clear space showing the residual, broken-down polynuclear leukocytes. Below there are a number of giant cells, and surrounding the clear space numerous endothelioid or angioblast cells.

leukocytes from the periphery toward the center, a picture resulting that closely resembles miliary tubercles (Figs. 80 and 81). In the center of such areas are broken down leukocytes and pyknotic nuclei. No organisms have been demonstrable. Still later even the disintegrated nuclei (Fig. 80) disappear, the giant cells atrophy somewhat and a nodule is produced completely made up of the altered angioblasts (endothelioid) and giant cells (Fig. 82). Although the giant cells may persist for a long time, this tissue is finally converted into the fibrillar variety, into which new vessels do penetrate (Fig. 83). The rapidity with which this conversion may take place is readily understood when those specimens are studied in which, side by side, in contiguous tributaries, the older and early process can be followed.

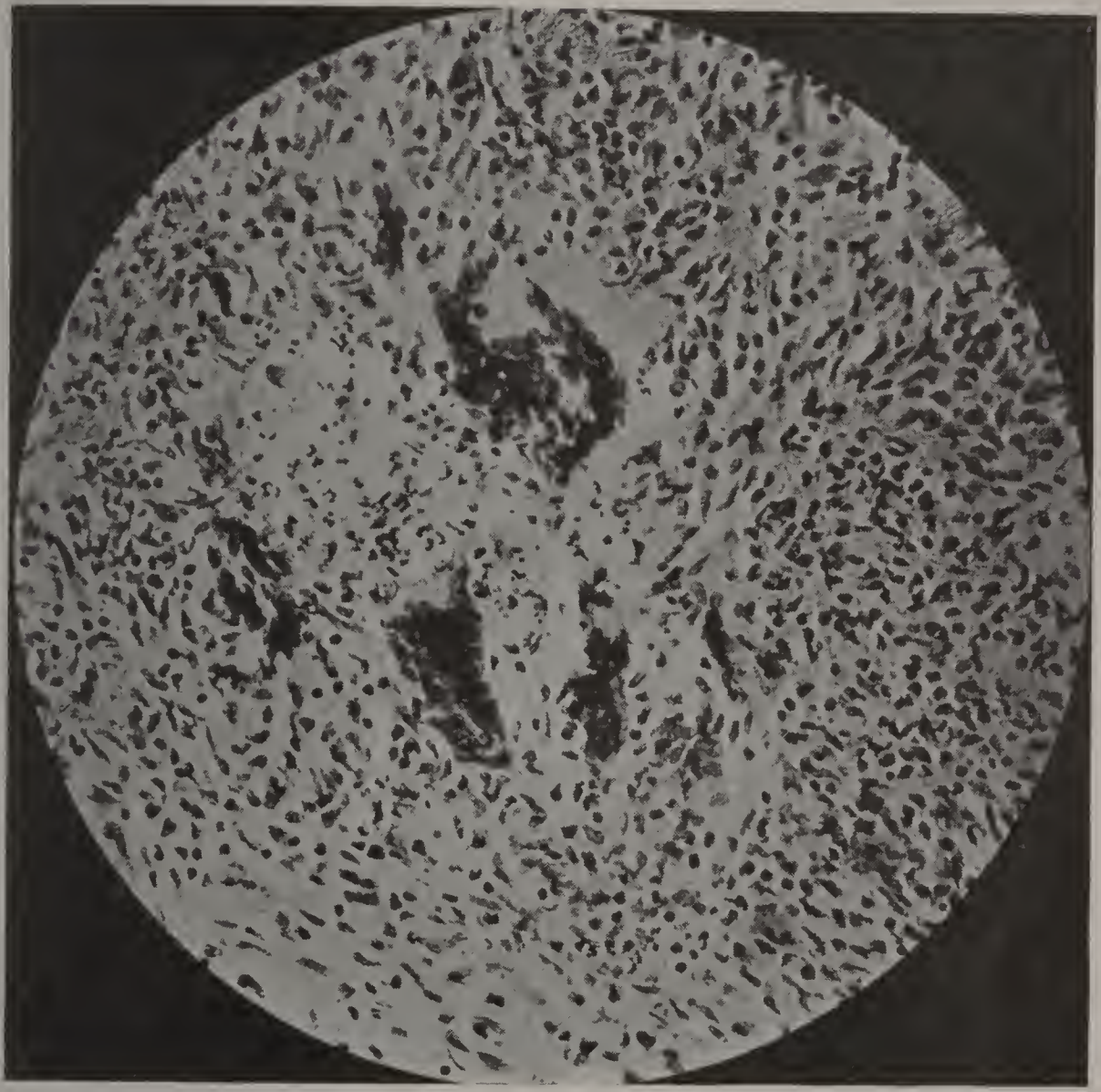


FIG. 80.—Old giant cell focus going on to healing; very few leukocytes remain.

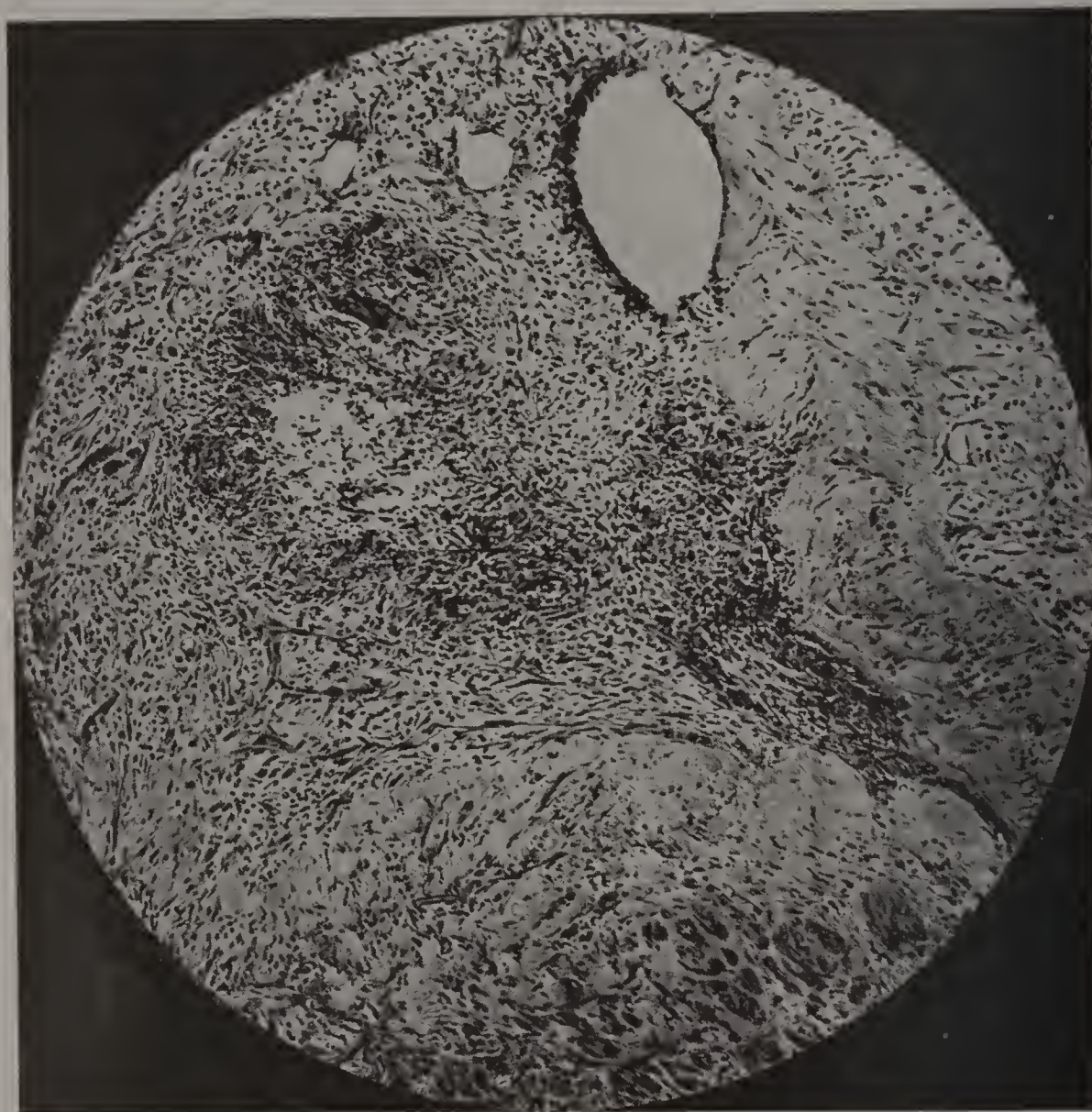


FIG. 81.—Miliary giant cell focus resembling tuberculosis in obturating clot found in vein of the forearm. Below and on the right side, valves of the vein; above and on the left, organization well advanced, tuberculoid focus retaining its characteristic appearance.

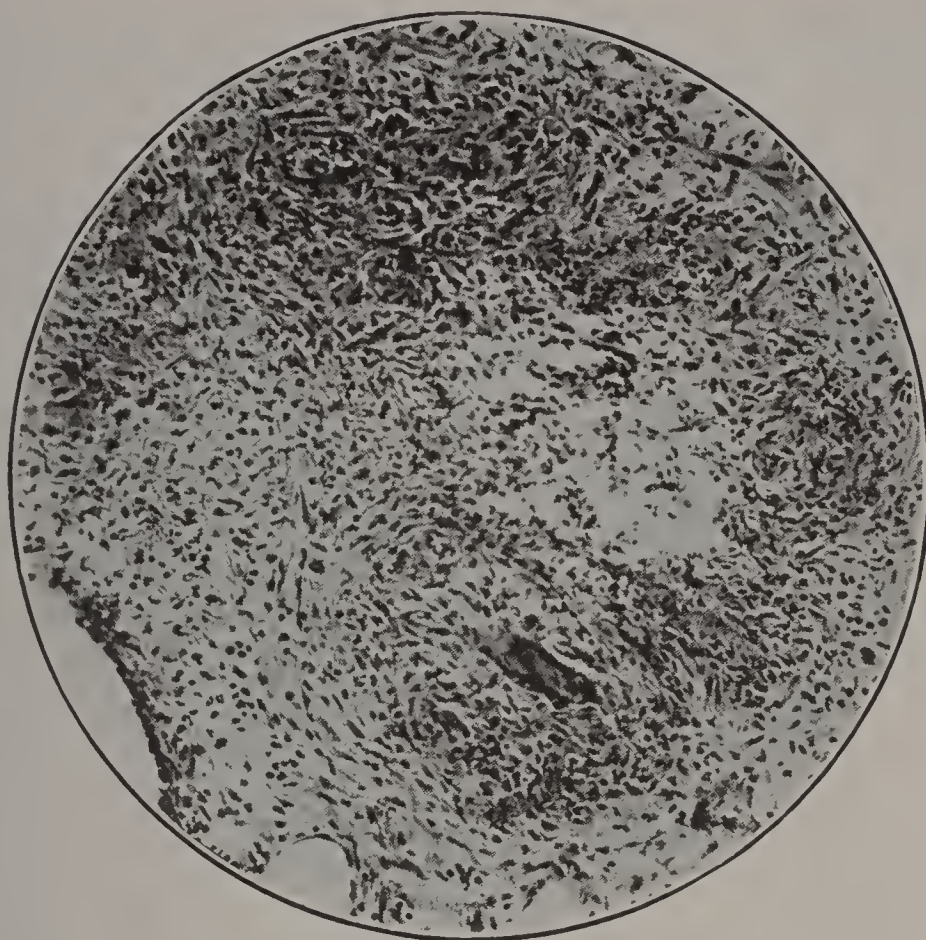


FIG. 82.—Later stage in "acute lesion," simulating miliary tubercle; endothelioid cells and giant cells surrounding focus of disintegrating leukocytes.



FIG. 83.—Vascularization (in the middle), proliferation of angioblasts and connective tissue around the purulent focus (above); older tissue below.

The Specific Lesion in the Deep Vessels.—If we turn to a consideration of the vessels in which the earliest lesions were best represented, we will be apprised of the interesting circumstance that the morphological alterations are such as apparently occur only in this disease. Certain foci containing giant cells, endothelioid cells, leukocytes and disintegrated nuclei are found lying usually in the periphery of a red or mixed clot. These areas strikingly resemble tubercles, and, in our experience, have been regularly diagnosticated as such by the uninitiated.



FIG. 84.—Acute lesion in a large artery. The middle coat is infiltrated with leukocytes, the clot showing miliary foci.

The Acute Lesion in the Deep Vessels.—It was possible to study these in the arteries and veins of three amputated lower extremities, where extensive, acute, inflammatory alterations were present in the popliteal, posterior tibial, and peroneal arteries and veins.

In one of the posterior tibial vessels of large caliber depicted in Fig. 84 the distribution of at least two purulent miliary foci in the obturating clot, and the diffuse inflammatory infiltration of the walls of the vessel are clearly represented. Under greater magnification the intensity of the cellular invasion and proliferation between the muscle fibers of the vessel wall can be well seen in Fig. 85, where the giant cells can also be discerned in the obturating thrombus.



FIG. 85.—Acute lesion in posterior tibial artery. On the left a portion of the media, and on the right a portion of the inflammatory clot are shown. Fibers of the media on the left are separated by inflammatory cells (leukocytes). On the right there are miliary inflammatory foci with giant cells in the clot.



FIG. 86.—Acute lesion in deep artery.

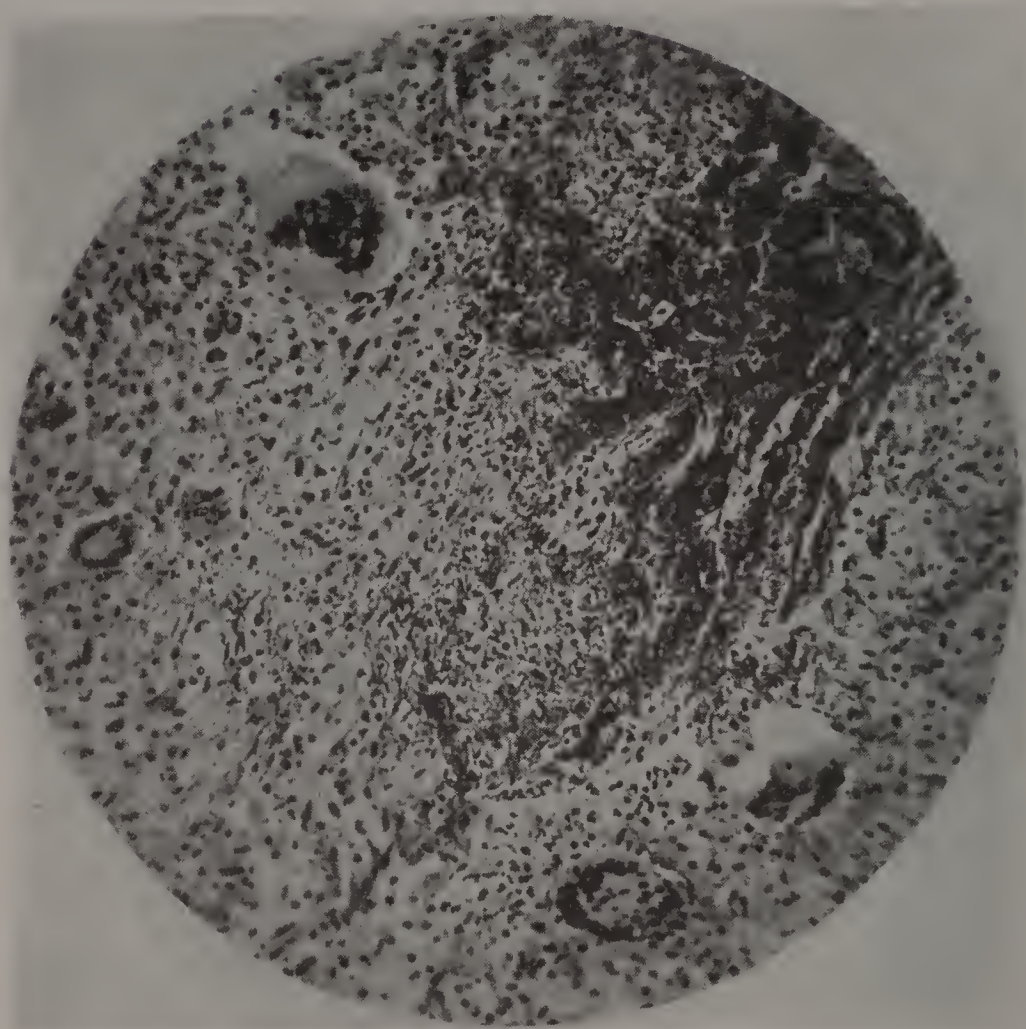


FIG. 87.—Acute lesion, a portion of a clot in an artery showing the acute lesion of thrombo-angiitis obliterans. At 1 or 2 o'clock the dark area is made up of fibrin; above and to the left, giant cells.

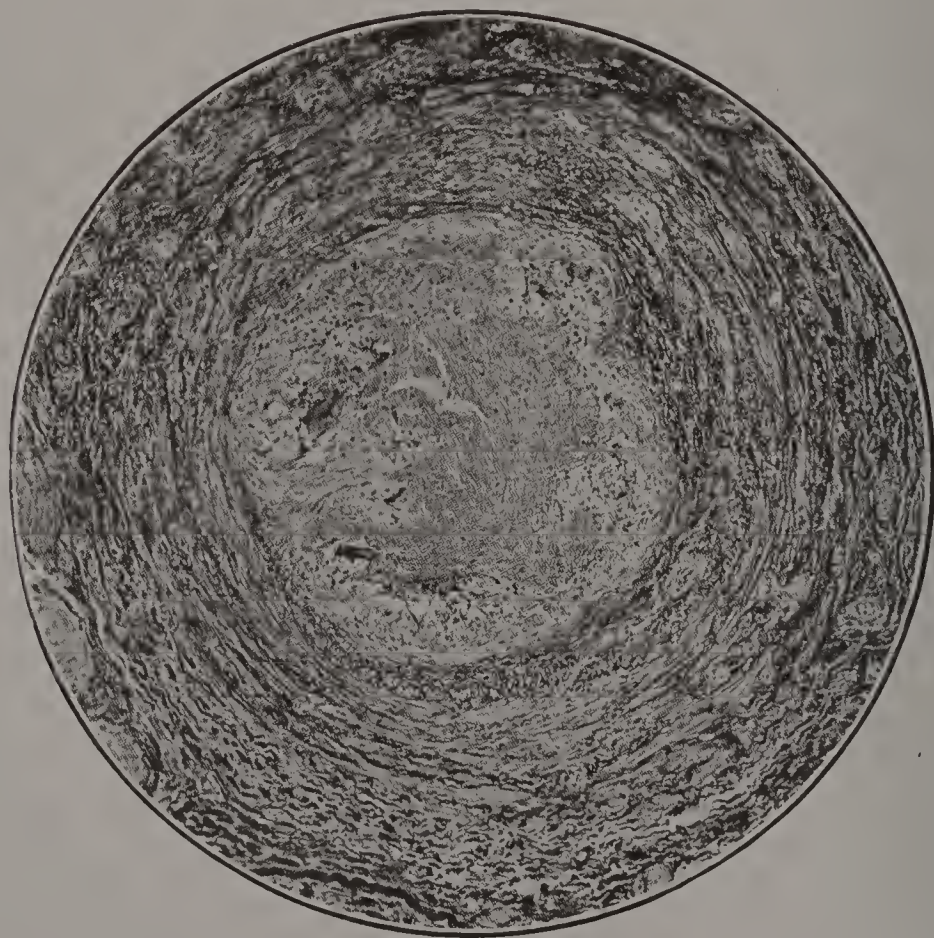


FIG. 88.—Early stage in a deep vein. The media is infiltrated with leukocytes, the lumen is filled with clot, in the periphery of which there are miliary giant cell foci.

In a still larger posterior tibial vessel there is less dispersion of the muscle fibers of the media, but the clot itself shows an exquisite illustration of the grouping of the miliary foci along its periphery (Fig. 86).

The formation of the giant cells can be studied in the deep vessels as well as in the superficial veins. An illuminating picture is one found in a posterior tibial artery, where the purulent focus almost came in contact with the inner wall of the vessel. In Fig. 77 the angioblasts can be seen migrating into the focus, and pass imperceptibly over into a syncytial body whose termination is a giant cell. Some of the later stages of organization in, and in the neighborhood of the miliary abscesses where the giant cells are taking on their older forms are illustrated in Fig. 87.

The disposition of a number of miliary foci in a deep vein is shown in Fig. 88, and the crowding together of the specific elements and reactive response into one section of the clot are exemplified in Fig. 89.

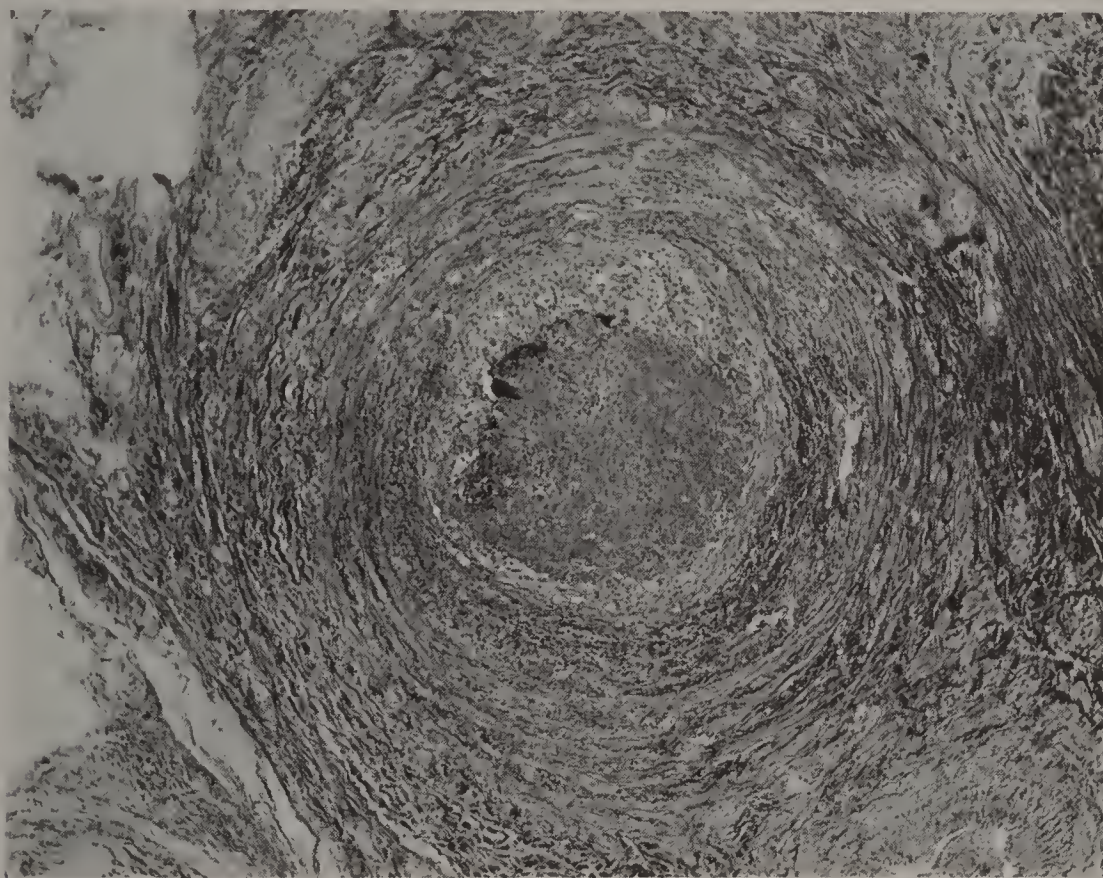


FIG. 89.—Peculiar disposition of giant cells in clot.

The Intermediate Stage of Healing.—Only a very few examples of the types of tissue evolved in the organization of the clot can be offered as examples here. Characteristic in the earlier stages are the multiplicity of cells, the large amount of pigment, the diffuse distribution of the small capillaries interspersed with blood pigment. Later there develops a relative preponderance of young connective tissue with consecutive dilatation of some of the canalizing capillaries, and the development of elastic tissue around the new-formed vessels *pari passu* with increasing age. Depending partly upon the shape and character of the clot, the fortuitous grouping of the canalizing vessels, the eccentric disposition of some clots, the retraction of these from the vessel walls, larger or small sinuses may be developed. These give the obturating tissue a fenestrated appearance, or make it semilunar on cross-section. The latter pictures can be confused with endarteritis obliterans, when organization is complete.

In Fig. 90 the rich cellular substitution of the clot, the interspersed capillaries, and the dark areas of blood pigment are the active response which has for its purpose the obliteration of the clot with connective tissue. The character of the cells is also shown in Fig. 91, where only a part of the organizing tissue has been reproduced.

Some of the later pictures with the enlarging blood vessels, the disappearance of many of the cells and the increase of young connective tissue can be studied in Fig. 92.



FIG. 90.—Intermediate stage of organization; on the left a portion of the media and the internal elastica; on the right, the cellular obturating tissue.

The formation of larger spaces or sinuses is depicted in Figs. 93 and 94. In the former organization is complete, only a part of the vessel wall being shown. On the right a portion of the occluding tissue with its smaller and larger vessels, its capillaries obliterated by connective tissues, and two sinuses of moderate size are not unusual appearances (Fig. 93). A higher magnification of the tissue in another case, (Fig. 94) shows that these sinuses may occasionally be lined with endothelium and filled with blood. Later, however, their walls are fortified by the deposition of elastic fibers.

The "Healed" or Old Stage.—For a thorough comprehension of the pathology as it presents itself in most of the vessels obtainable from an amputated limb—the "old" or "healed" stage is the most instructive. The most common lesion is a total obliteration of the lumina of arteries and veins by vascular connective tissue. A study of the development of this connective tissue shows that the end product may be extremely varied

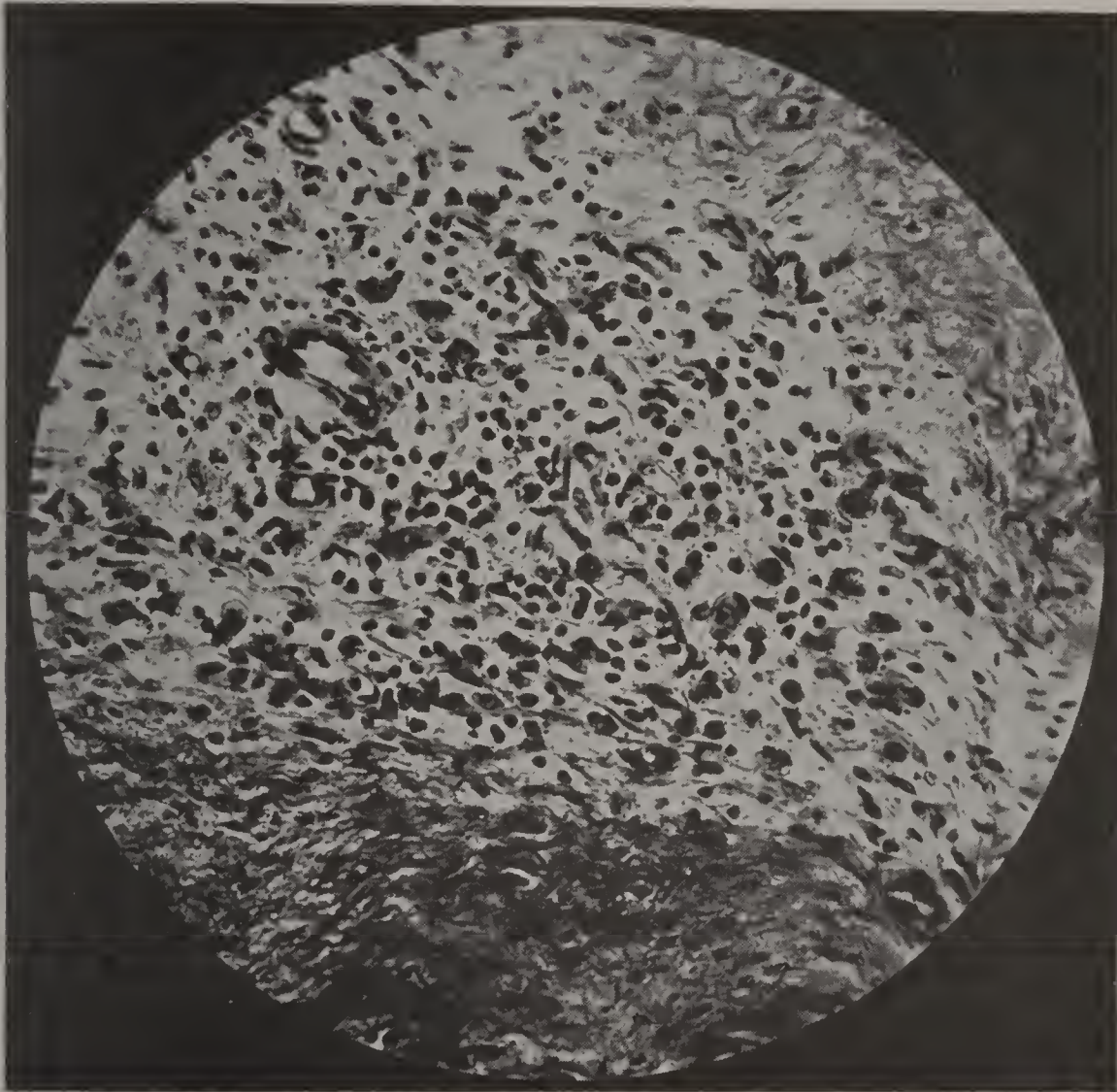


FIG. 91.—Cellular intermediate stage of the organizing process.



FIG. 92.—High power picture of one variety of end result in the process of organization of the clot, the vessels and pigment being striking features.

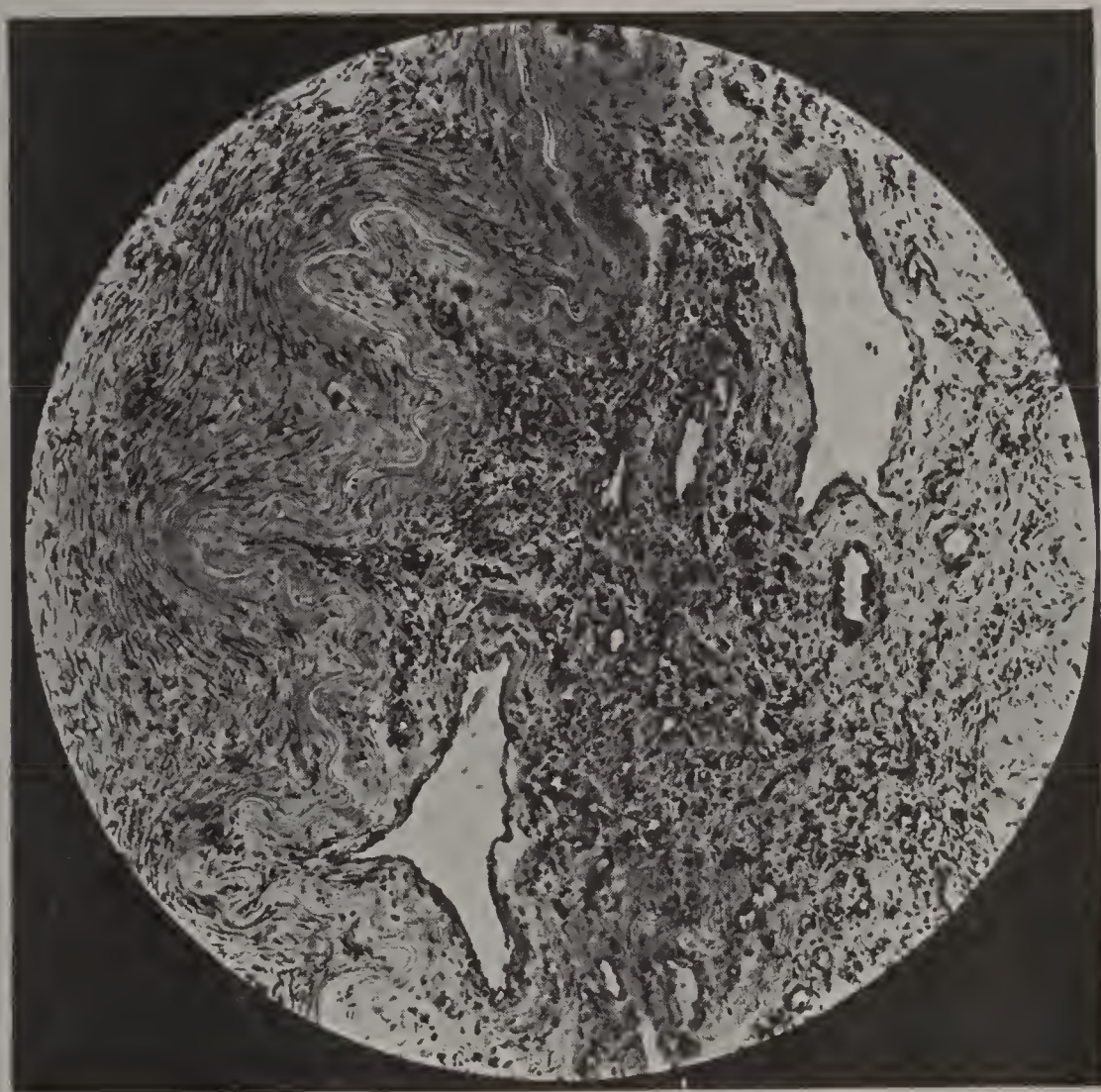


FIG. 93.—Fenestrated occluding tissue on the right with two large sinuses; on the left a part of the middle coat with the fluted internal elastic membrane running from above downward.

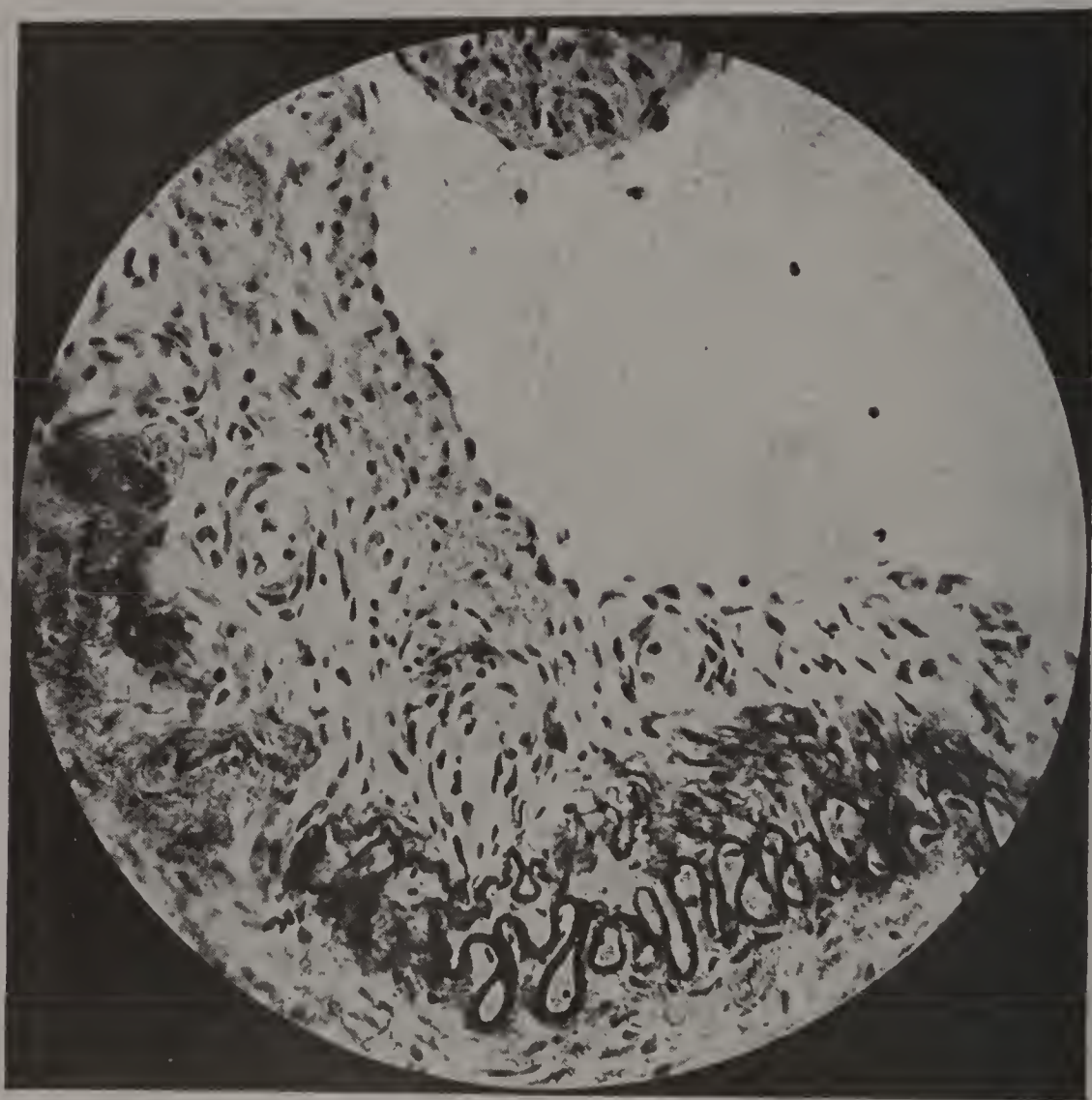


FIG. 94.—A type of obturating tissues enclosing a large blood sinus and smaller capillaries. The internal elastic membrane on the left is partly disorganized and well preserved on the right below.

in its general appearance, but that each picture can be interpreted correctly as having its origin in the lesion of occlusive thrombosis. Thus the vessels may be filled with connective tissue harboring numerous small vessels, much pigment containing hemosiderin, with a fair amount of connective tissue cells; or, the cellular elements and vessels may be but sparsely represented, dense sclerotic fibrous tissue with but an occasional sinus predominating.

Another interesting variant of the terminal stages of occlusion and one which is more apt to affect the smaller arteries (such as the *dorsalis pedis* and *dorsalis hallucis*) is reproduced in Fig. 95. Here the new vessel formation in



FIG. 95.—Old healed stage in small artery, artery converted into a cord containing dense fibrous tissue and vessels.

the organized clot is striking, and the vascularization of the media can be well seen. The penetration of the media by new vessels and the proliferation of the small vessels in this coat have been described elsewhere, and need only be mentioned here as evidence of the attempt at organization of the clot and of the establishment of a supplementary circulation.

The occlusion of the popliteal artery by the completely organized tissue in which every vestige of inflammatory product has been resorbed, a multitude of canalizing channels only remaining, is portrayed in Fig. 96. In contrast to this a very small artery may also be completely obliterated into a cord of bizarre appearance, because the canalizing vessels have become so markedly hypertrophied (Fig. 95).

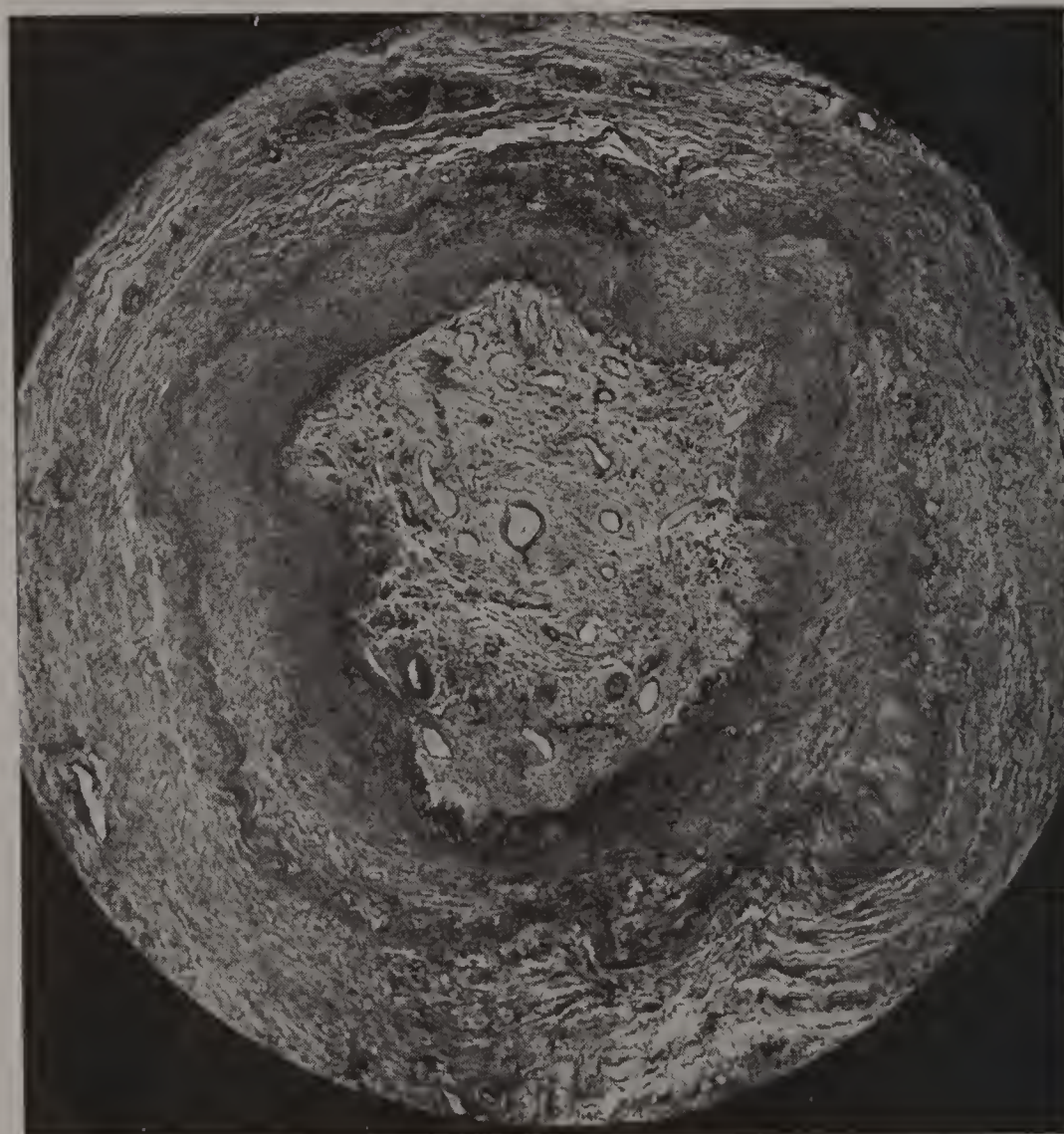


FIG. 96.—Popliteal artery occluded by vascularized connective tissue, pigment, small vessels, and capillaries being features.

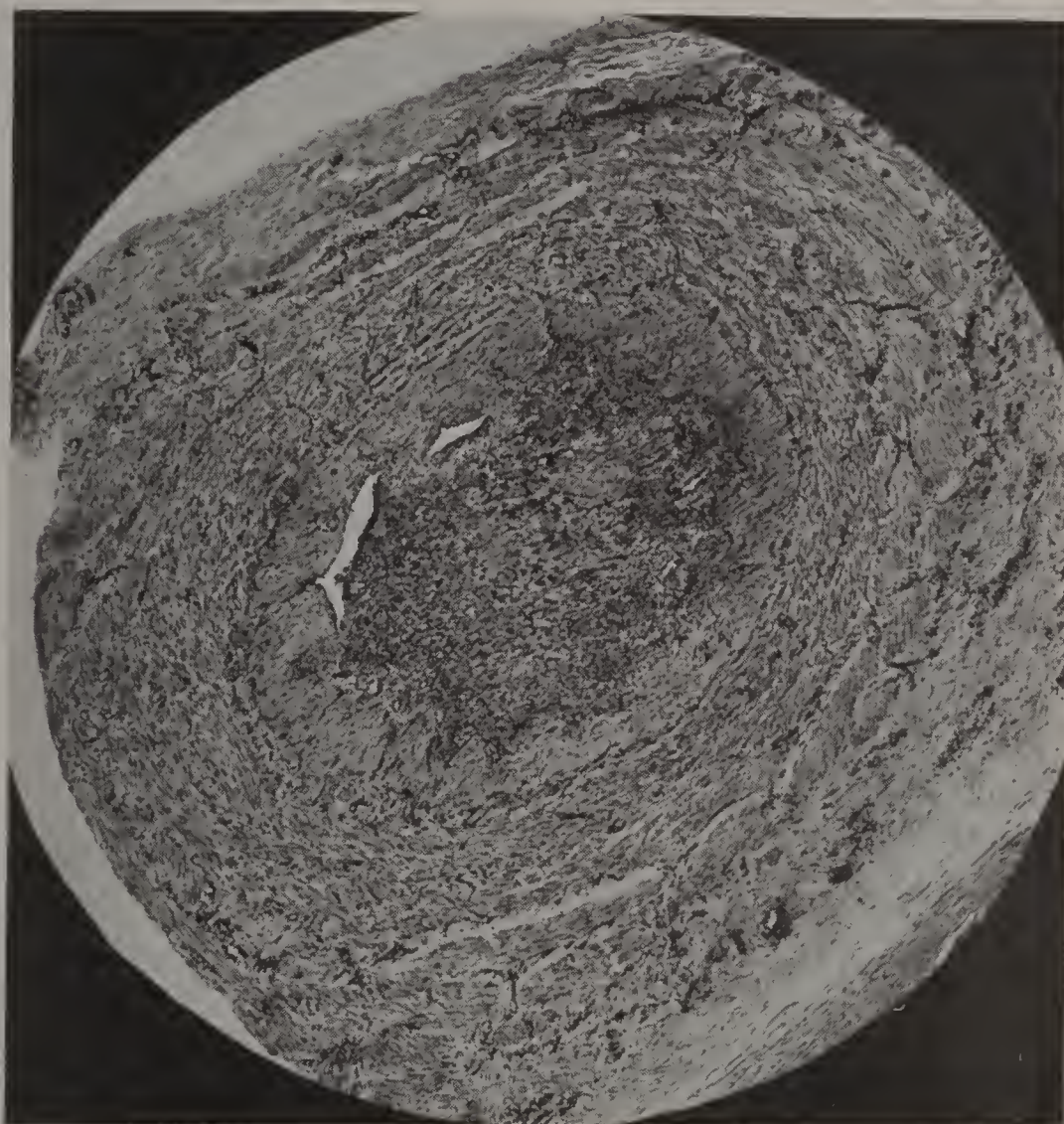


FIG. 97.—Old type of organized clot showing cicatricial contraction of the connective tissue, and occlusion and compression of the cellular elements, also secondary thickening of the intima.

With increasing age, changes in the intima may occur that show themselves as diffuse thickening, and the vessels contract about the obturating tissue, the latter becoming more and more firm (Fig. 97). This cicatrization may go on to such an extent as to give confusing products, in that the hypertrophy of the intima may lead to erroneous interpretation. The contraction of the obturating tissue mass, the enlargement of the intimal layers and the diffuse fibrosis about the vessels extending well into the fatty tissues about the arteries can be studied in Fig. 98.

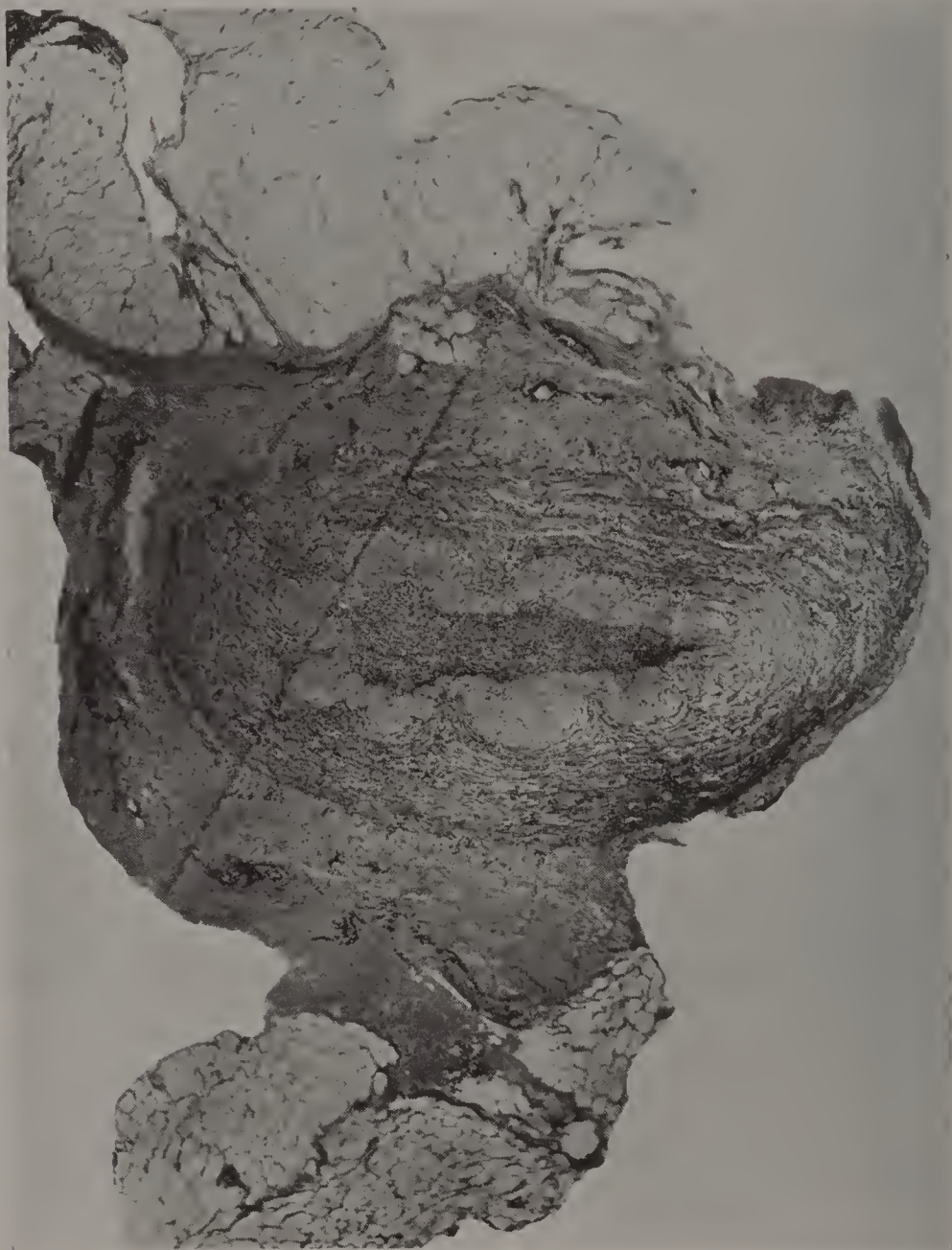


FIG. 98.—Contracted type of closed artery. The lumen is narrowed and filled with fibrotic tissue. The intima shows hyaline degeneration and is thickened following the thrombotic process.

In the older stages in which there is but a sparse distribution of the cells in the cicatrizing mass, the veins are apt to show less contraction than the arteries. So in a vein shown in Fig. 99, the irregular sinuses that canalize the occluding mass are in sharp contrast to the more rigid and contracted process in the cribriform arterial sections shown in Fig. 100.

Again in the artery in Fig. 101, where a central lumen is simulated by a narrow canalizing channel, the retraction of the internal elastica with corresponding constriction of the artery is well shown. Fig. 102 is an interest-



FIG. 99.—Old sclerotic occluding tissue in a vein.

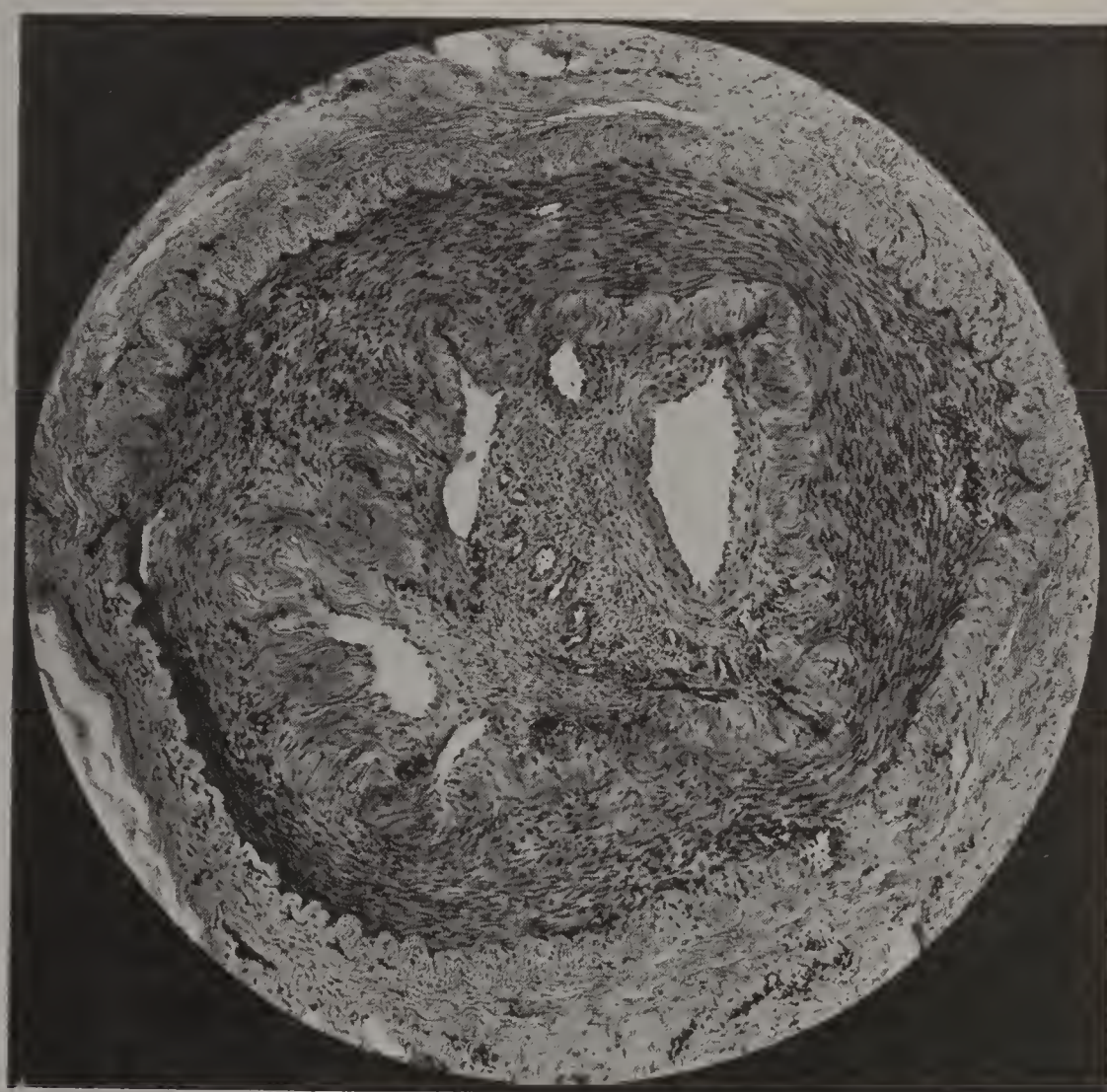


FIG. 100.—Old or healed type of lesion with large canalizing vessels.



FIG. 101.—Obliterating tissue, old variety in dorsalis pedis, can be mistaken for “endarteritis;” old connective tissue, canalization; only slight vascularization of media.

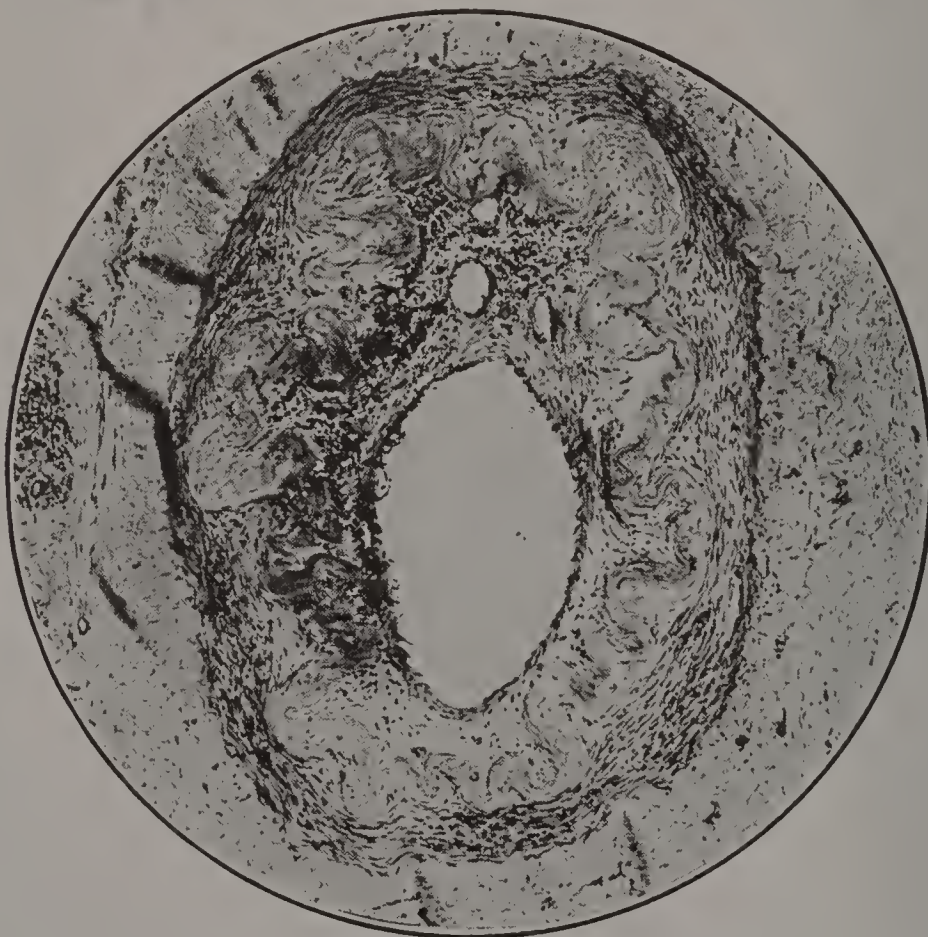


FIG. 102.—“Old” occlusion in artery simulating “endarteritis obliterans;” eccentrically situated large canalizing vessel (below) crowding rest of tissue to one side (above in illustration).

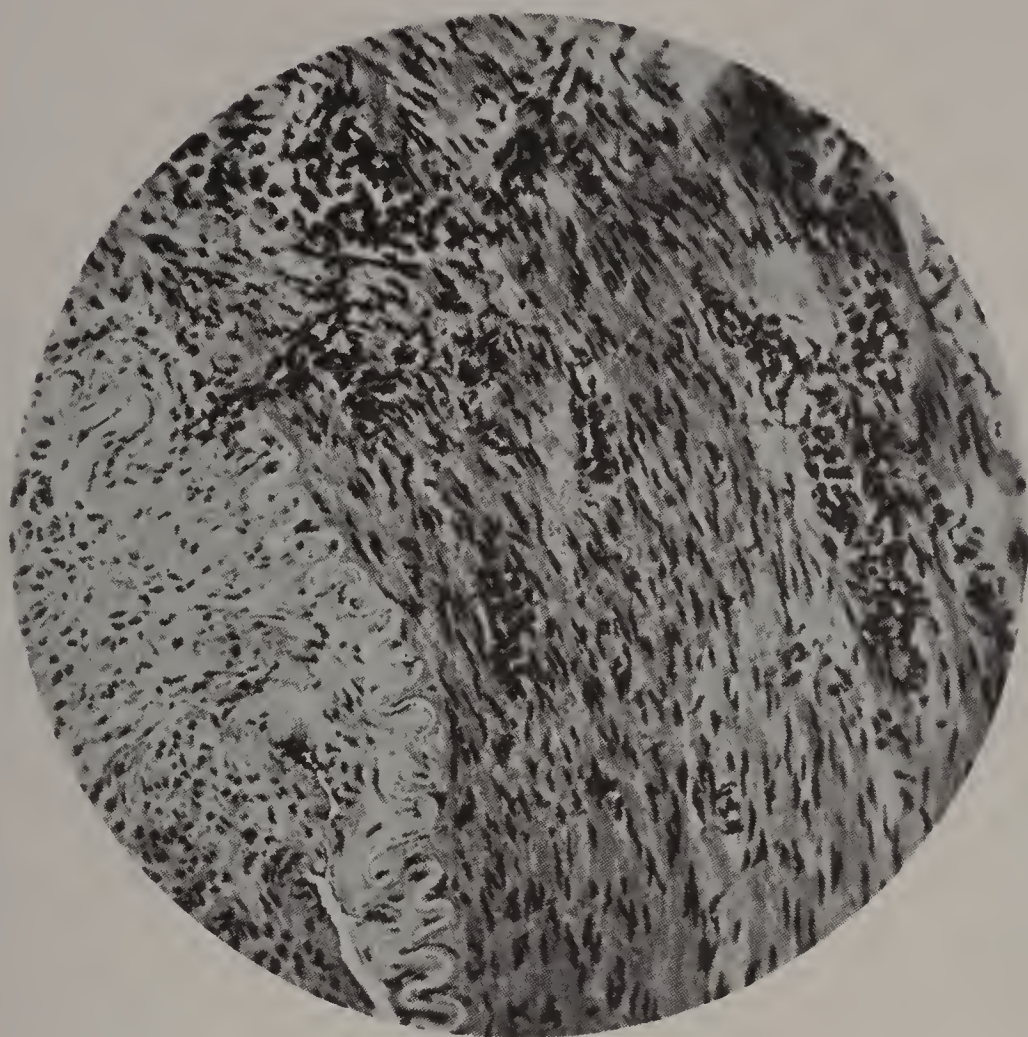


FIG. 103.—Lesions of the media in medium sized arteries; many capillaries with or without slight perivascular lymphoid infiltration in the media; penetration of the internal elastic lamina by vessels which enter rather old typical occluding tissue.

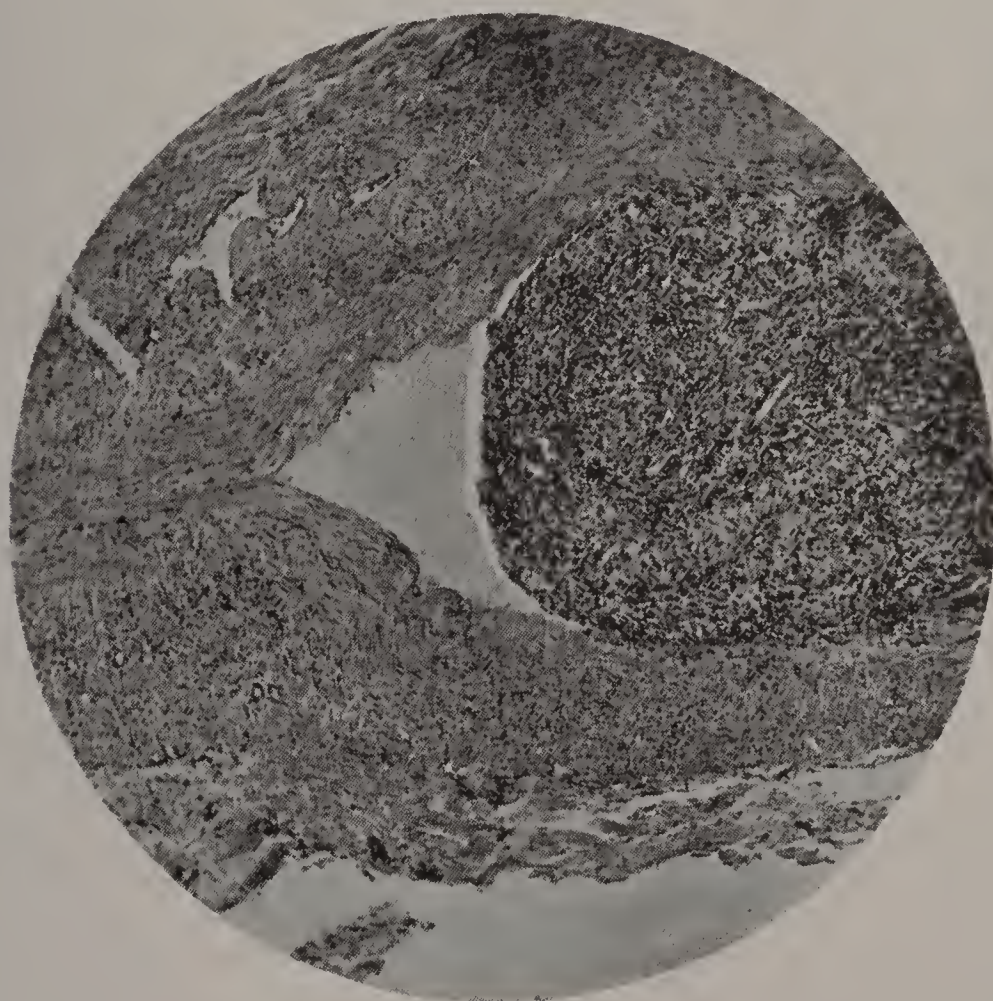


FIG. 104.—Longitudinal section of an artery containing termination of organized clot; to the left the arterial walls are normal, collapsed and in contact; to the right, occluding tissue.

ing illustration of an eccentrically placed canalized channel that crowds the organized clot into the small crescentic mass on the right and is an example of the formation of pictures that can be mistaken for endarteritis obliterans.

The change that is left in the media in the healed stage, besides connective tissue infiltration and atrophy, is the diffuse invasion with new formed vessels (Fig. 103). Although this process is most pronounced in thromboangiitis obliterans, it can be also observed in atherosclerotic processes, whenever secondary thrombosis occurs, or whenever there is marked degeneration, calcification or bone formation in the walls.



FIG. 105.—Termination of the red clot in a vein. It is adherent at 3 o'clock, and in the media at this site there is inflammatory infiltration.

Terminations of the Occluding Tissue.—Studying some of the terminations of the occluding tissue in arteries and veins, we not infrequently encounter a rounded convex projection looking upward (cephalad), abruptly ending the obturating plug, and often lying in and just below an apparently healthy vessel wall (Fig. 65). At other times the old occluding tissue seems capped by a more recent pyramidal or tapering clot, which appears grossly and microscopically to be deposited by mere accretion (stagnation clot). When we view the former type, as illustrated in the longitudinal section (Fig. 104), we can well understand the nature of the pathological change. Here there can be no doubt as to the thrombotic nature of the process. The accretion or stagnation clots, on the other hand (Figs. 105, 106, and 107), present a somewhat different picture, not varying from that of thrombosis and organization induced by other causes.



FIG. 106.—Bland termination of accretion clot in vein with healthy wall. (See Fig. 105.)

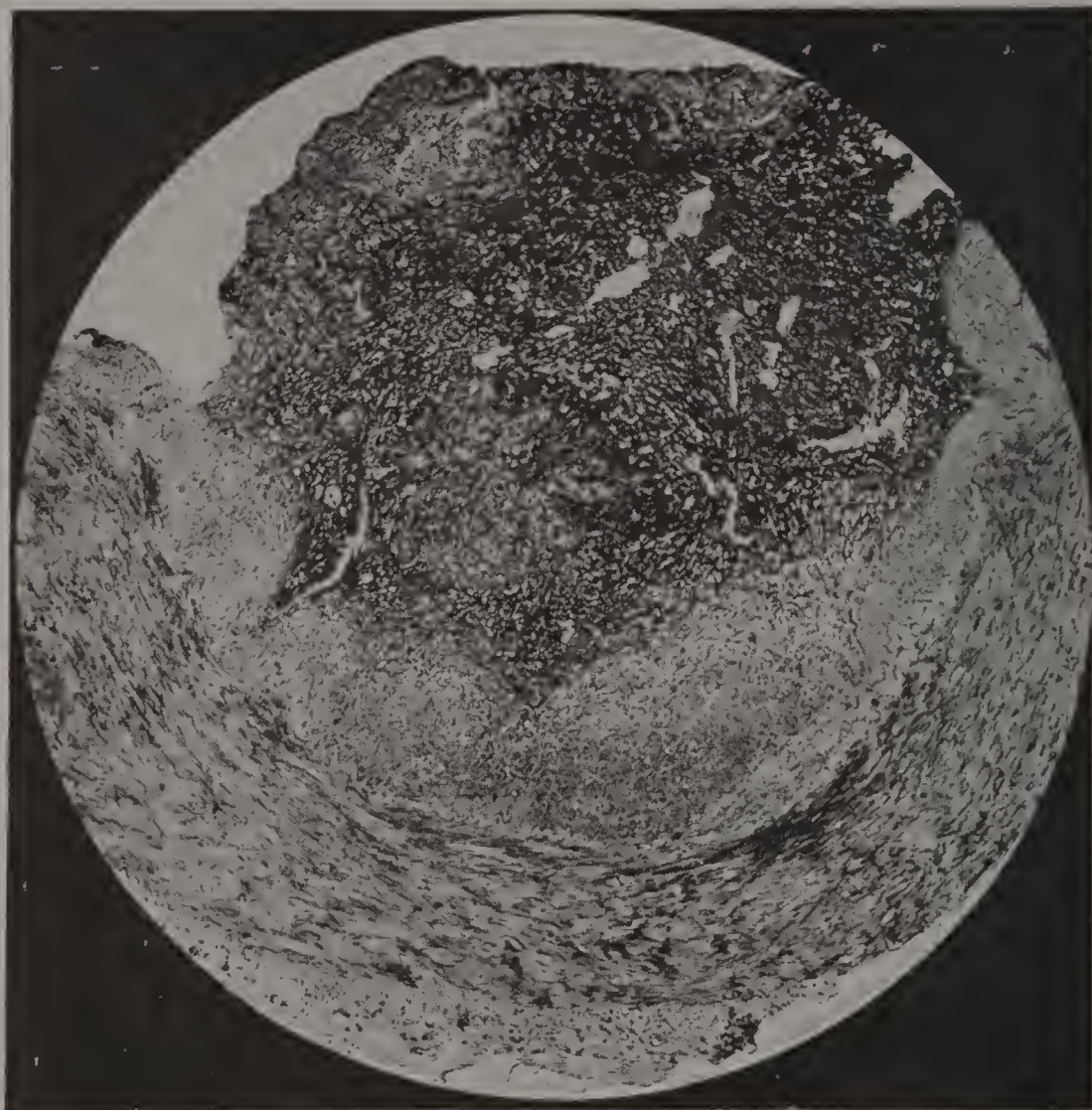


FIG. 107.—Termination of clot in an artery the seat of atherosclerotic disease; good example of associated lesions.

In Fig. 104 the rounded termination of the obturating mass is seen lying in a vessel cut longitudinally, and whose walls are collapsed just beyond the organized clot. The latter presents the usual picture of the old stage with connective tissue vessels and pigment. A parietal termination in a vein is seen in Fig. 108.

The accretion clot may be either abruptly separated from the specific, or may pass imperceptibly into it. When the latter is the case, the tapering termination may be found adherent to the wall in places, and it is there that evidences of the inflammatory nature of the process may still be present. In Fig. 105 such infiltration of the media and intima is seen where the clot is



FIG. 108.—Termination of obturating tissue in a vein in parietal form.

attached. If the media be infiltrated with migrating and polynuclear cells, we may conclude that the specific inflammatory process has extended into and emerges imperceptibly into the accretion clot. If the organizing process is the typical bland one, no such reaction in the media can be noted.

Fig. 106 shows sections made somewhat nearer the apex of the clot, the vessel being absolutely healthy in this region.

When such a termination occurs over an atherosclerotic or thickened intima, confusing pictures may result after organization has taken place (Fig. 107).

In rare instances terminations of the clot may adhere in a parietal fashion to the walls of the vessels, as shown in the vein in Fig. 108.

The Pathology of the Relapsing Lesion.—Not only is the process a migrating one both in arteries and veins, but all of the constituents of a sheath may not be simultaneously affected. An old advanced lesion may be found in an artery or vein, an acute lesion in contiguous vessels. The finding of various stages of the disease in different members of the same vessel sheath is exceedingly instructive. This is well illustrated in Fig. 64.

Thus in Fig. 109 a large artery affords a view of the old lesion, as well as one of its *venae comites*. Another accompanying vein, however, is in the "acute" stage (Fig. 110) of the disease, a smaller venule or satellite being in

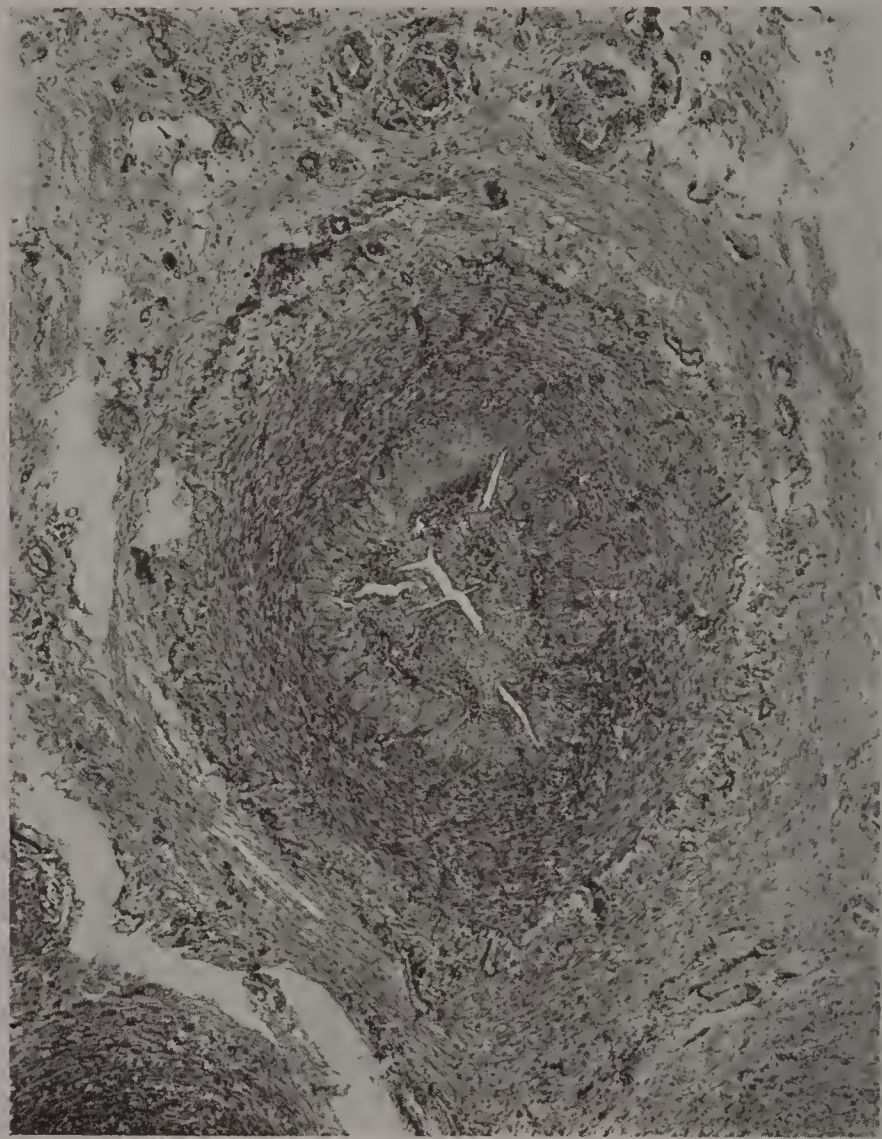


FIG. 109.—Old sclerotic occluding tissue in thrombo-angiitis obliterans; a high power magnification of this vessel being reproduced. (See Fig. 64.)

the intermediary stage, where certain "miliary giant cell foci" make their appearance (Fig. 111). Such pictures not only reveal the thrombotic nature of the disease, but also present an argument in favor of the following two assumptions: that the disease begins with an inflammatory lesion attended with occlusive thrombosis, and that it affects the arteries and veins in a sort of relapsing fashion, similar to that which occurs in the veins in migrating phlebitis.

Recurrences are found also in the deep vessels. In the popliteal vessel seen in Fig. 112, evidences of thromboses are found. The whole artery was doubtlessly affected by the acute process a long time since, for the lumen was filled with the old type of organized tissue, many capillaries and large blood sinuses, and thick walled canalizing vessels. One of these daughter canalizing

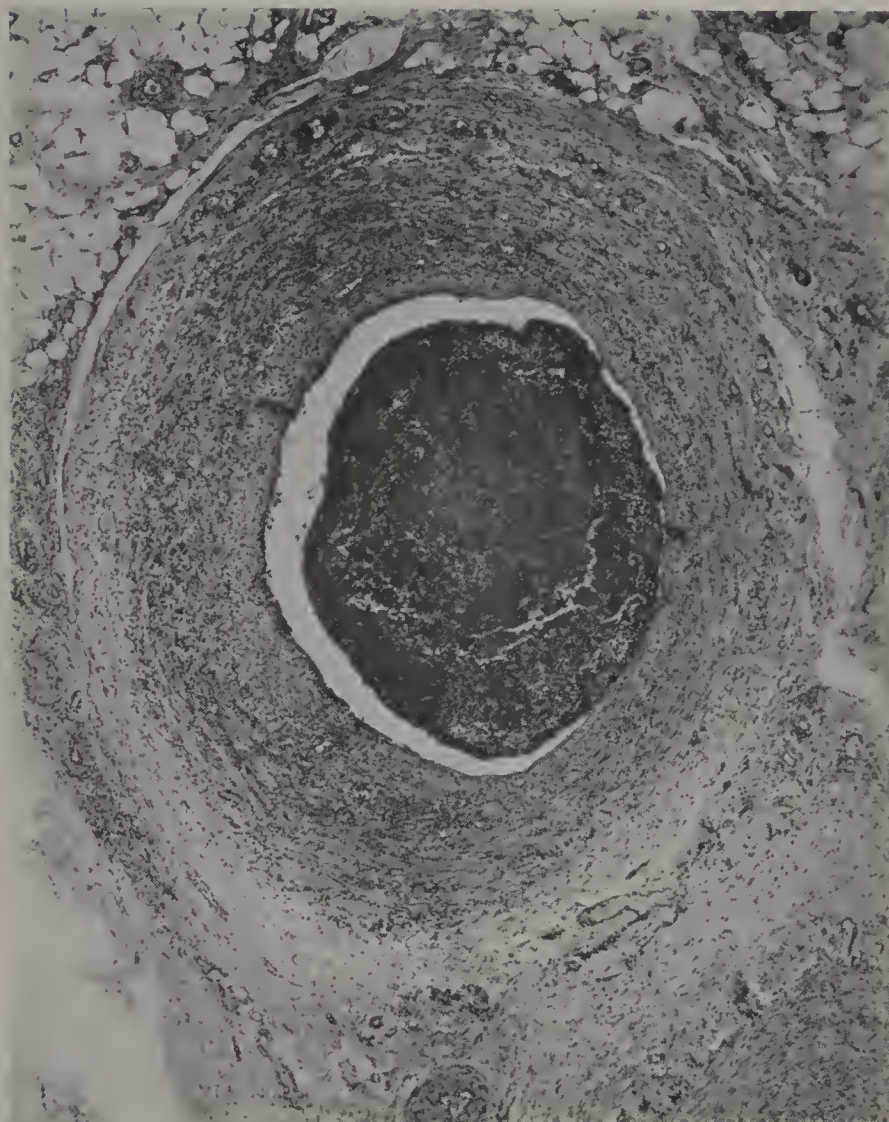


FIG. 110.—Acute stage in another of the veins seen in Fig. 64.

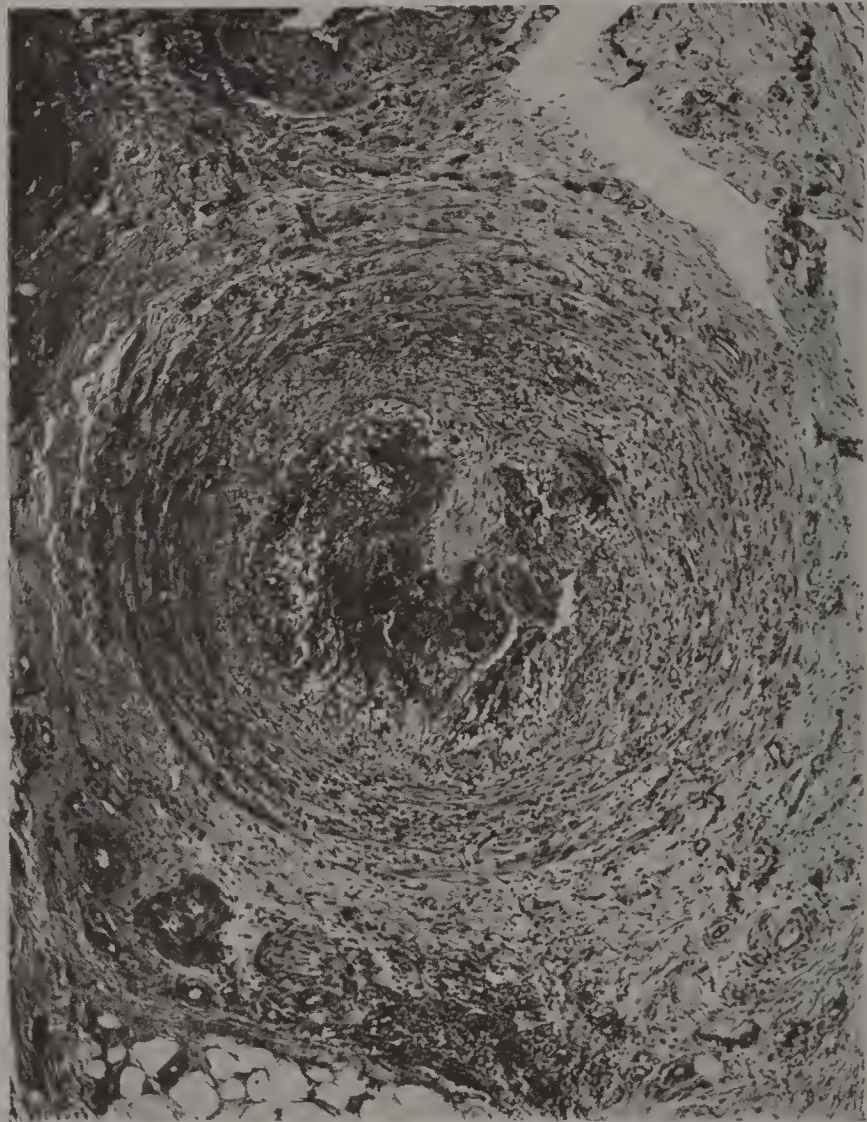


FIG. 111.—Miliary foci in an acutely inflamed vein in same sheath with preceding. (See Fig. 64.)



FIG. 112.—Relapsing acute stage in an artery already occluded and in the old stage on the left, giant cell focus.



FIG. 113.—High power of Fig. 112.

arteries shows the acute process within its walls, and a miliary giant cell focus. A high power view of this focus is seen in Fig. 113. Thus the combination of an old healed lesion with a recent superimposed acute inflammatory one in a daughter canalizing vessel is beautifully shown.

A similar instance of combined old and recent lesion in the peroneal artery is depicted in Fig. 114. Here the crescentic mass to the left in the picture shows the healed connective tissue stage, and in the eccentric lumen that is left, recent thrombosis, acute inflammation, and miliary giant cell foci are present.



FIG. 114.—Combined old lesion and recent acute lesion in an artery (peroneal). The peripheral portion of the obturating tissue is composed of vascularized connective tissue. On the right, the greater portion of the lumen, however, is occupied by a more recent clot with miliary foci.

The Elastic Tissue in Thrombo-angiitis Obliterans.—What information can be obtained from a study of specimens stained for elastic tissue?

Characteristic of the early stages of the metamorphosis of the obturating clot is the absence of elastic tissue, and also the absence of the excessive reduplication of the internal elastic layer so characteristic of arteriosclerotic processes. As the canalizing vessels become older, however, new formed elastic tissue disposes itself about them (Fig. 115) in concentric layers. The scant development of the elastic tissue in a popliteal artery completely filled with organized clot is seen in Figs. 116 and 117, where but the faintest indication of new elastic fibers is seen about some of the canalizing vessels. Where, however, there are small complicating plaques of arteriosclerosis, there the

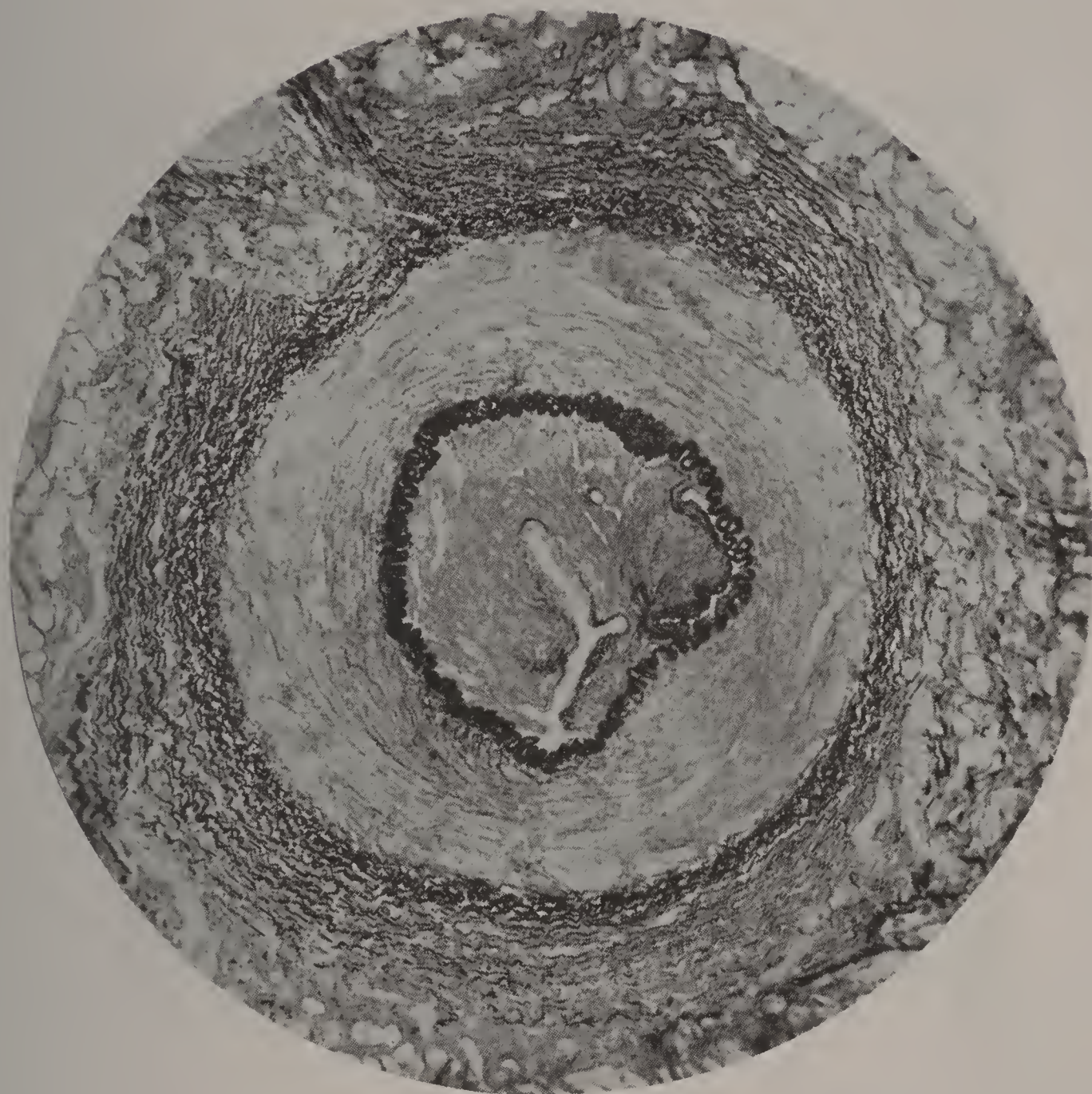


FIG. 115.—Elastic tissue stain of section of vessel shown in Fig. 101.

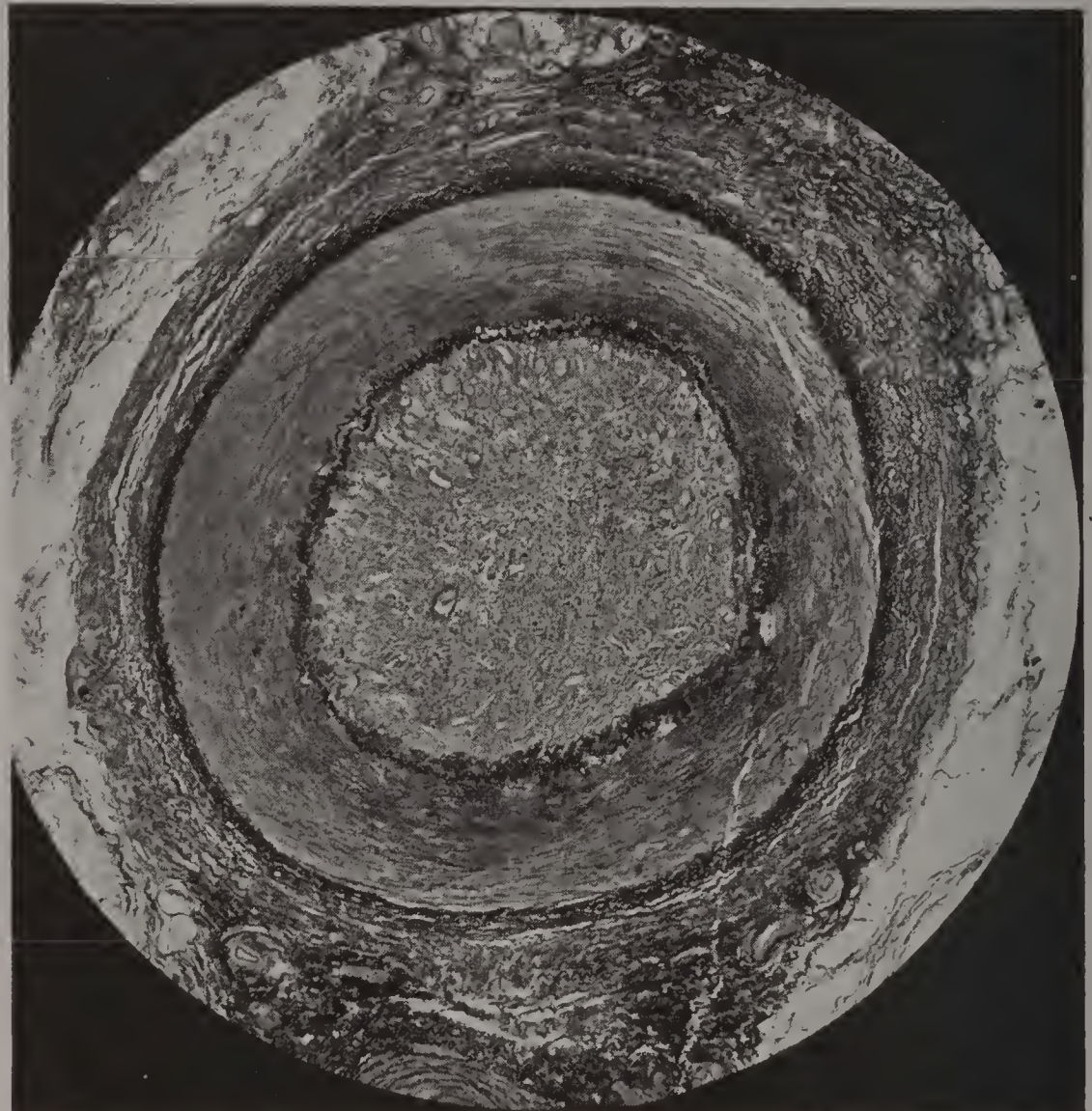


FIG. 116.--Occluding tissue devoid of elastic fibers in the popliteal artery.

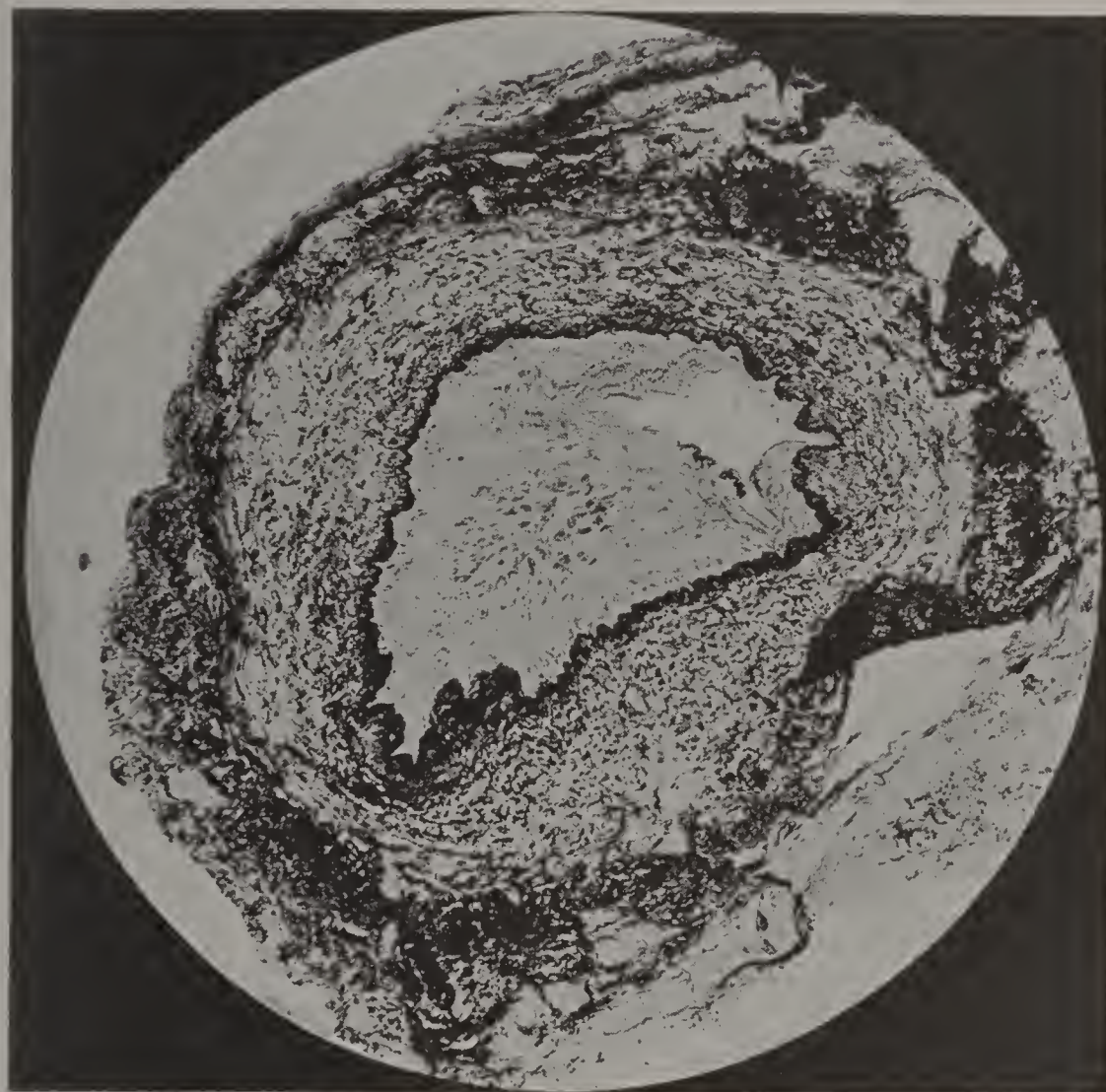


FIG. 117.—Elastic tissue but sparsely represented about the vessels of the occluding tissue in a vein.



Fig. 118.—Absence of elastic tissue in the clot; small atherosclerotic patch below in the intima of the artery.

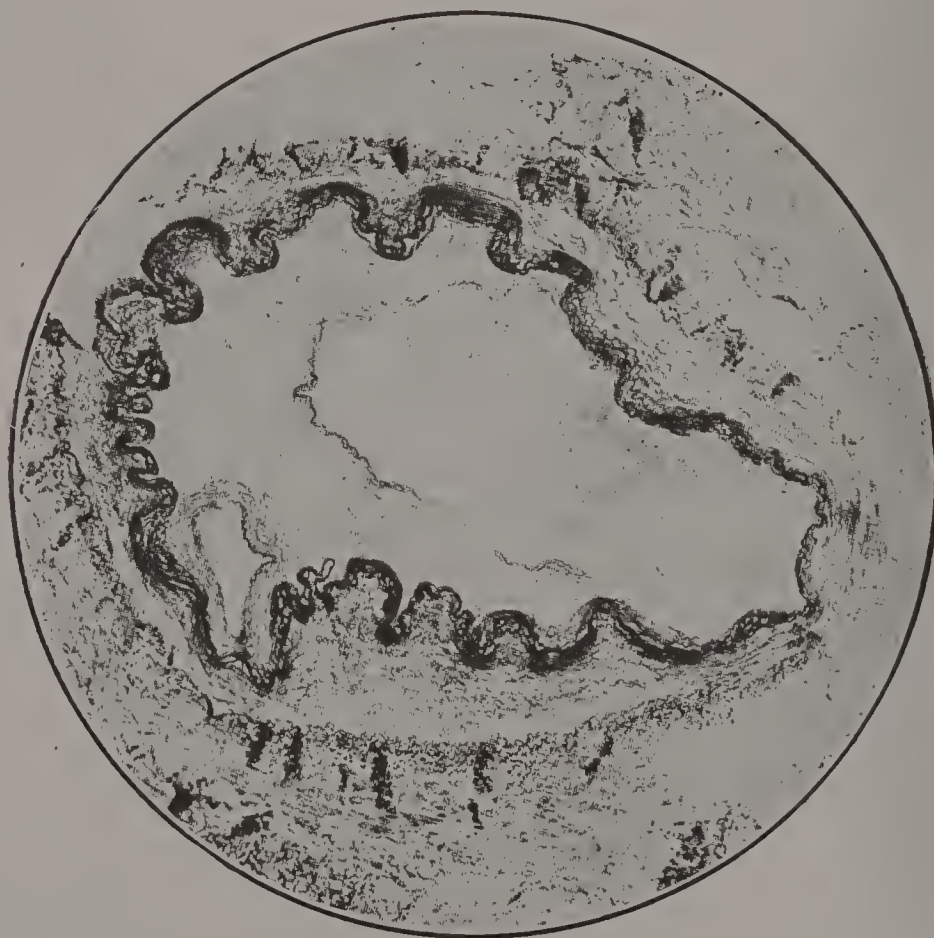


FIG. 119.—New lumen found in organized clot in vein simulating endarteritis obliterans (elastic tissue stain).

corresponding hyperplasia and duplication of elastic lamina take place (Fig. 118).

Serial sections stained with the elastic tissue method demonstrate clearly that the occasional pseudo-lumina (Fig. 119) found in arteries of thrombo-angiitis obliterans are but expanded or eccentrically placed canalizing sinuses which divide up into subsidiary branches and are traceable (Fig. 120) into numerous smaller canalizing vessels at different levels.

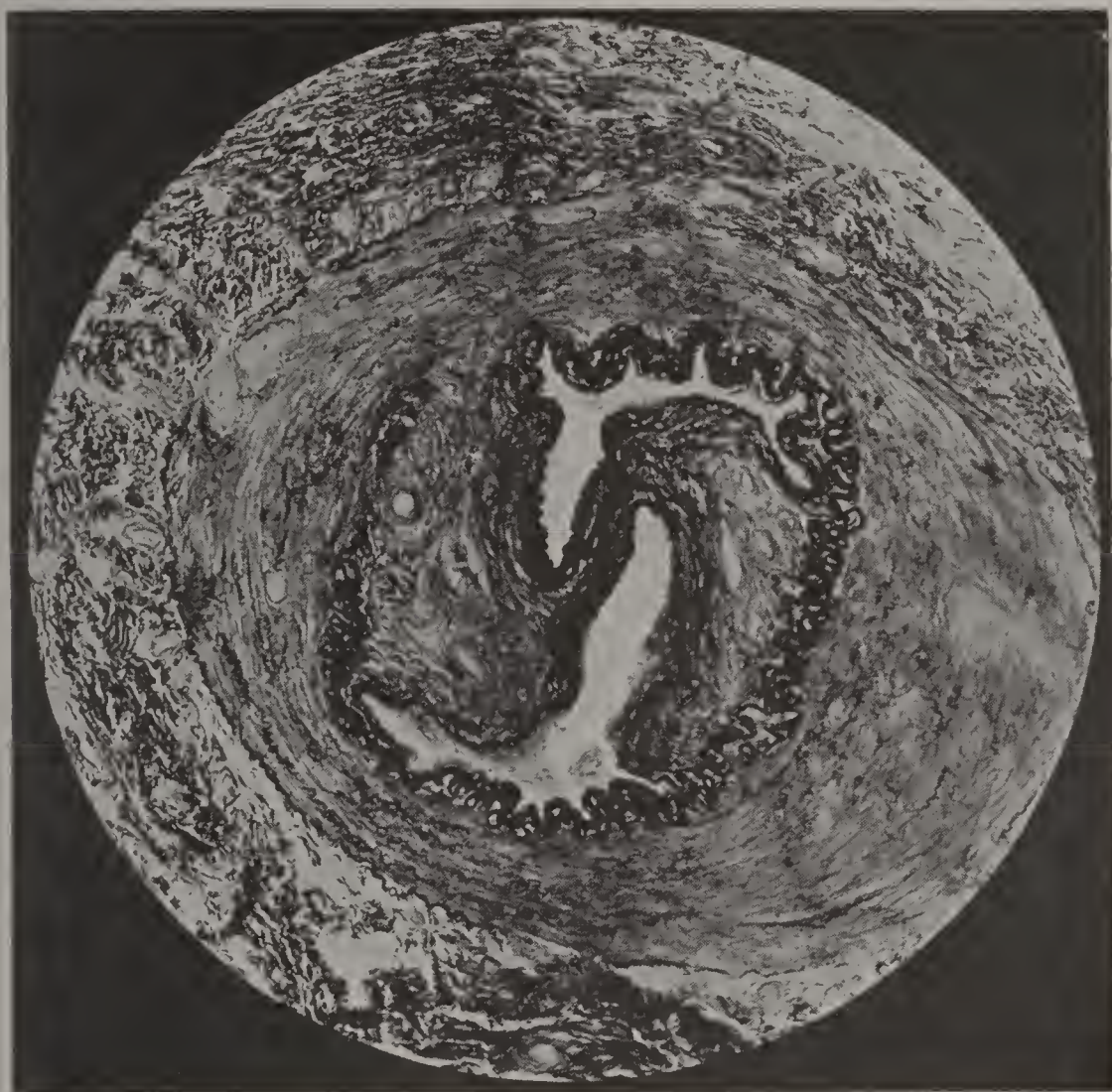


FIG. 120.—Septum formation due to the eccentric position of the two large canalizing sinuses.

In Fig. 120 the elastic tissue disposed about the two sinuses separated by a septum stamps these as new formations. Elsewhere they are found to divide into smaller canalizing vessels.

Other sections, such as are seen in Figs. 121 and 122, further demonstrate the new formation of elastica about a canalizing vessel.

Where, however, the lesion is one of long duration (years), a secondary thickening of the intima takes place with corresponding proliferation of elastic fibers that must not be confused with arteriosclerotic processes (Fig. 123).

True atherosclerotic plaques in which the elastic fibers are disposed more or less parallel with the internal elastica lamina and encroaching upon the lumen of the vessel may occur, *for the two diseases may be associated*. This is seen in Fig. 124, where such an atherosclerotic plaque occupies the crescentic portion of the right part of the lumen, whilst the occluding mass of thrombo-angiitis obliterans completes the recess left.



FIG. 121.—Elastic fibers about the sinus on the right in the clot.

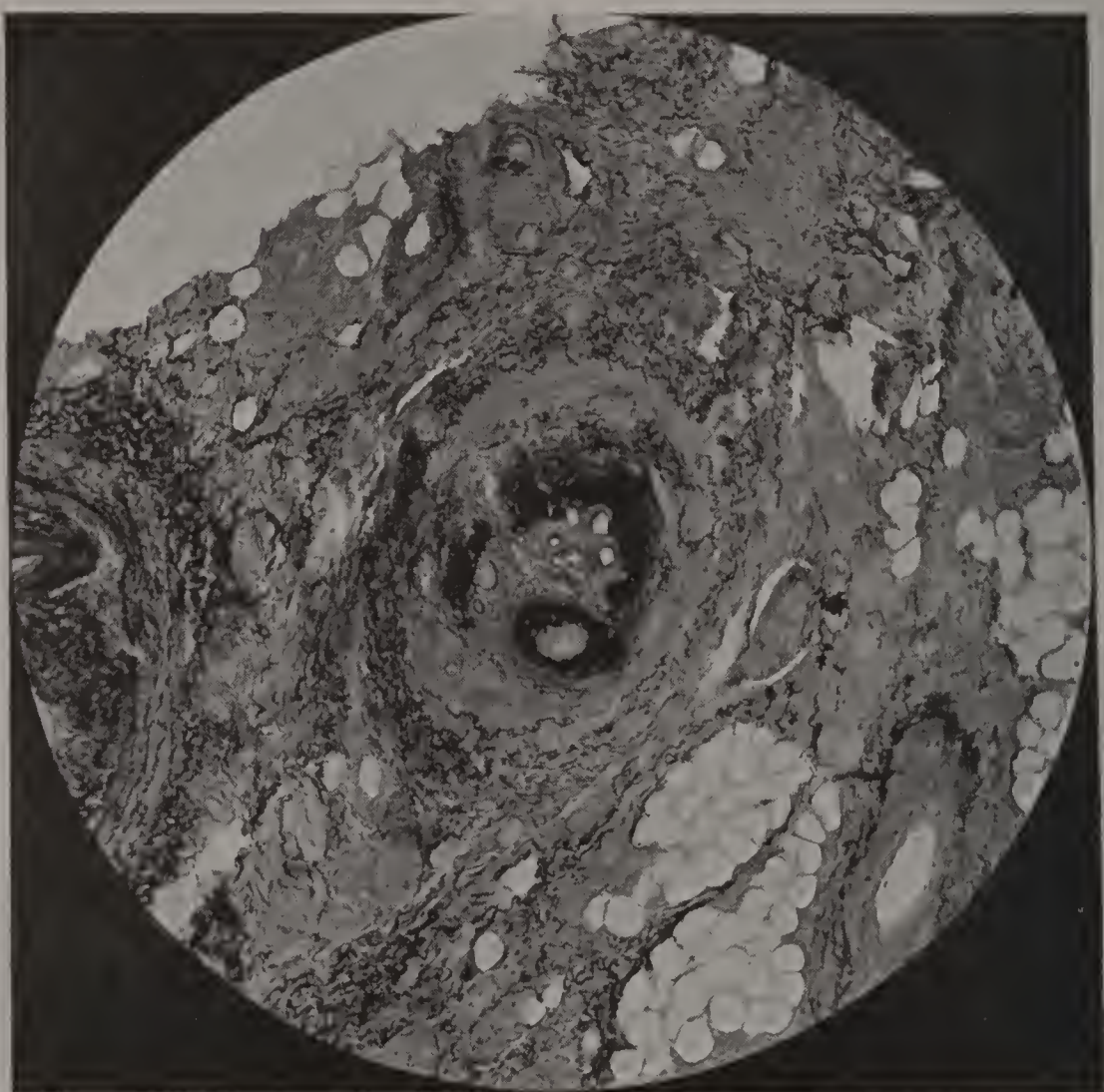


FIG. 122.—Perivascular disposition of new elastic fibers in the occluding organized clot.

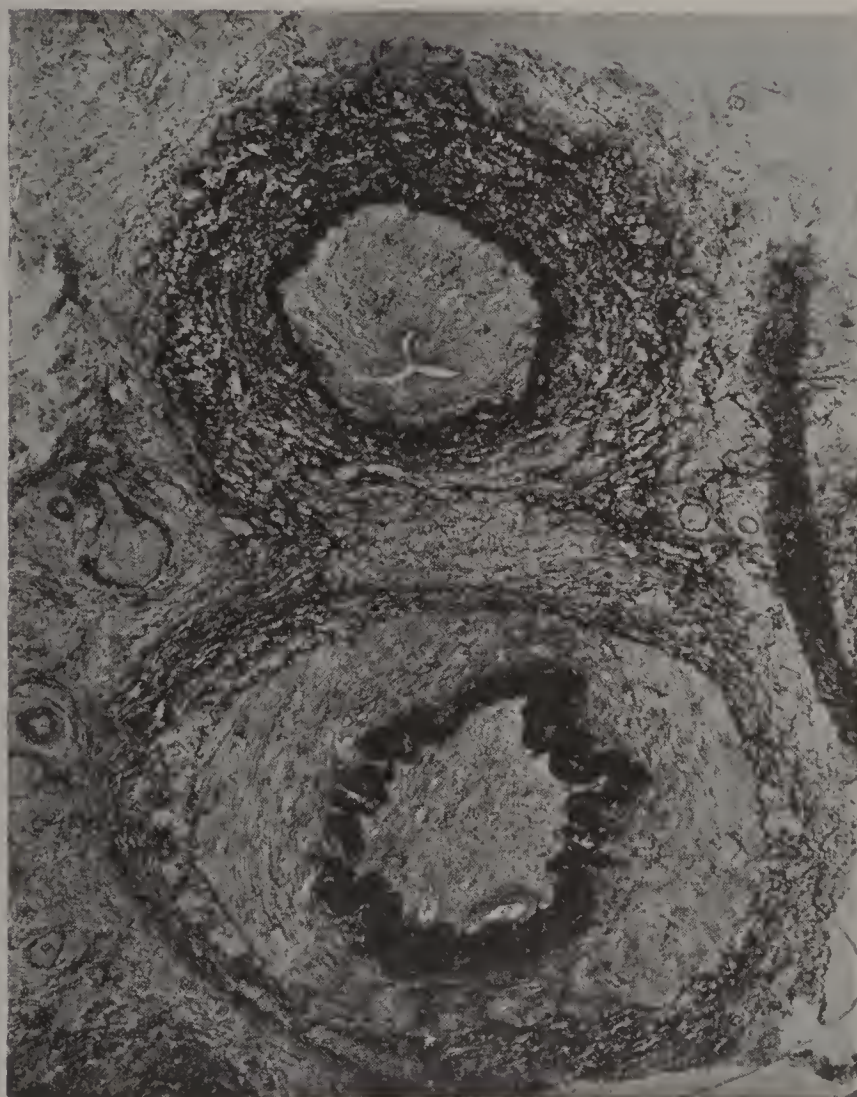


FIG. 123.—Relative absence of elastic fibers in the organized clot; secondary hyperplasia of the intimal elastica in the artery below.

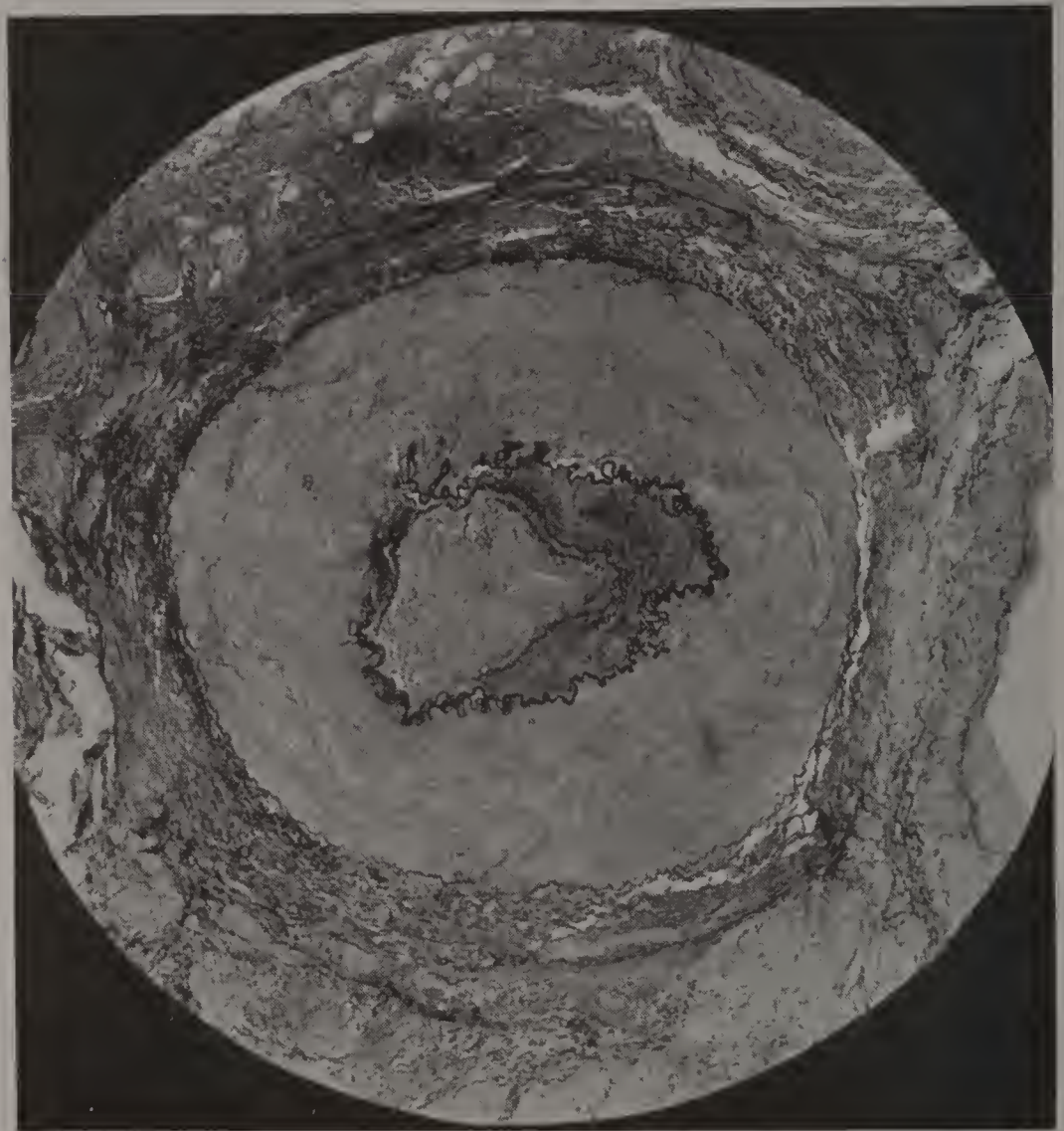


FIG. 124.—Old type of occlusion at site of an arteriosclerotic plaque on the right.

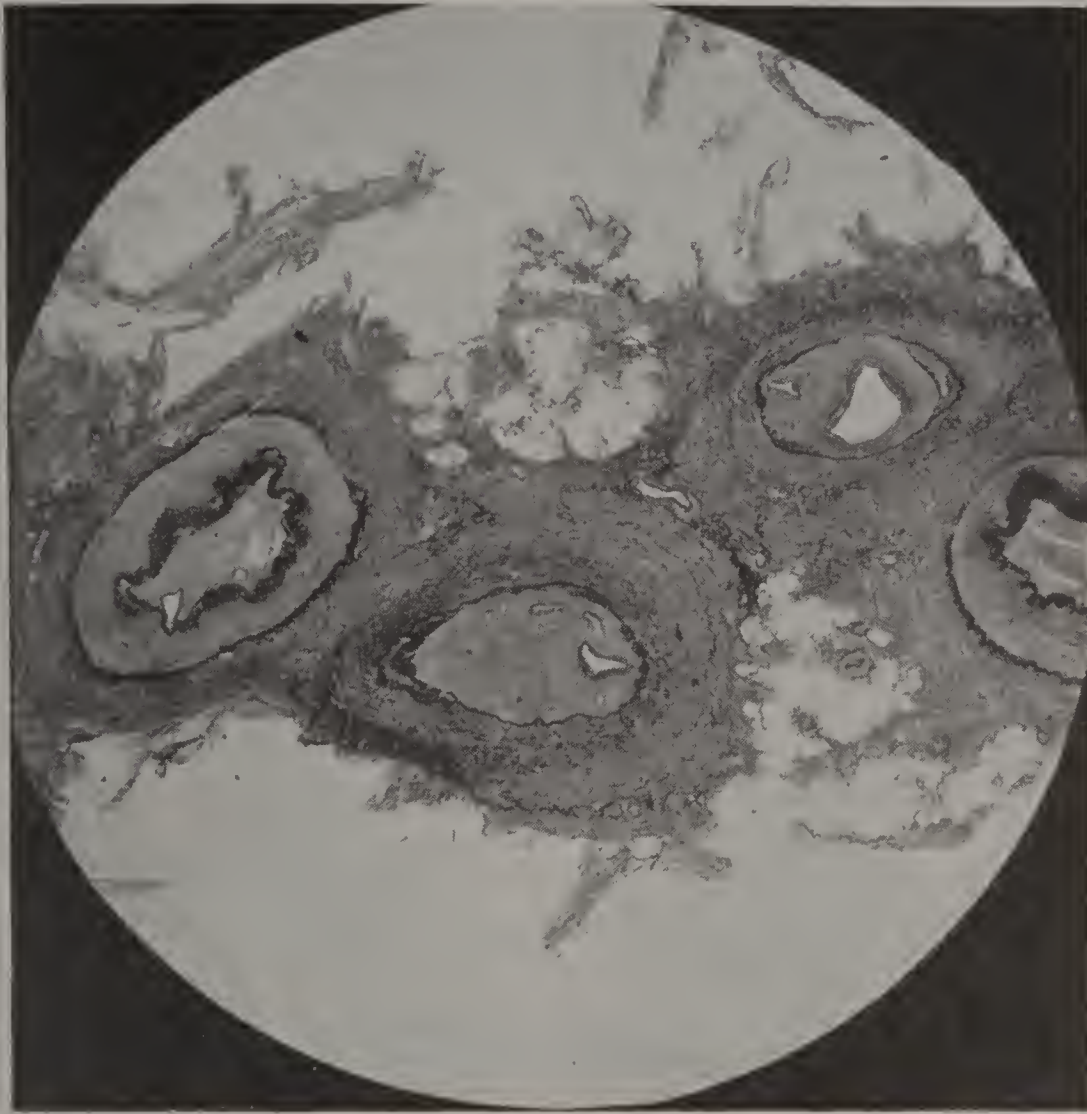


FIG. 125.—Elastic tissue stain showing old lesion in arteries and venæ comites; also picture in vein simulating endarteritis obliterans; on the left and right, arteries; in the middle two veins, the left with small, the right of the two with a large canalizing channel.

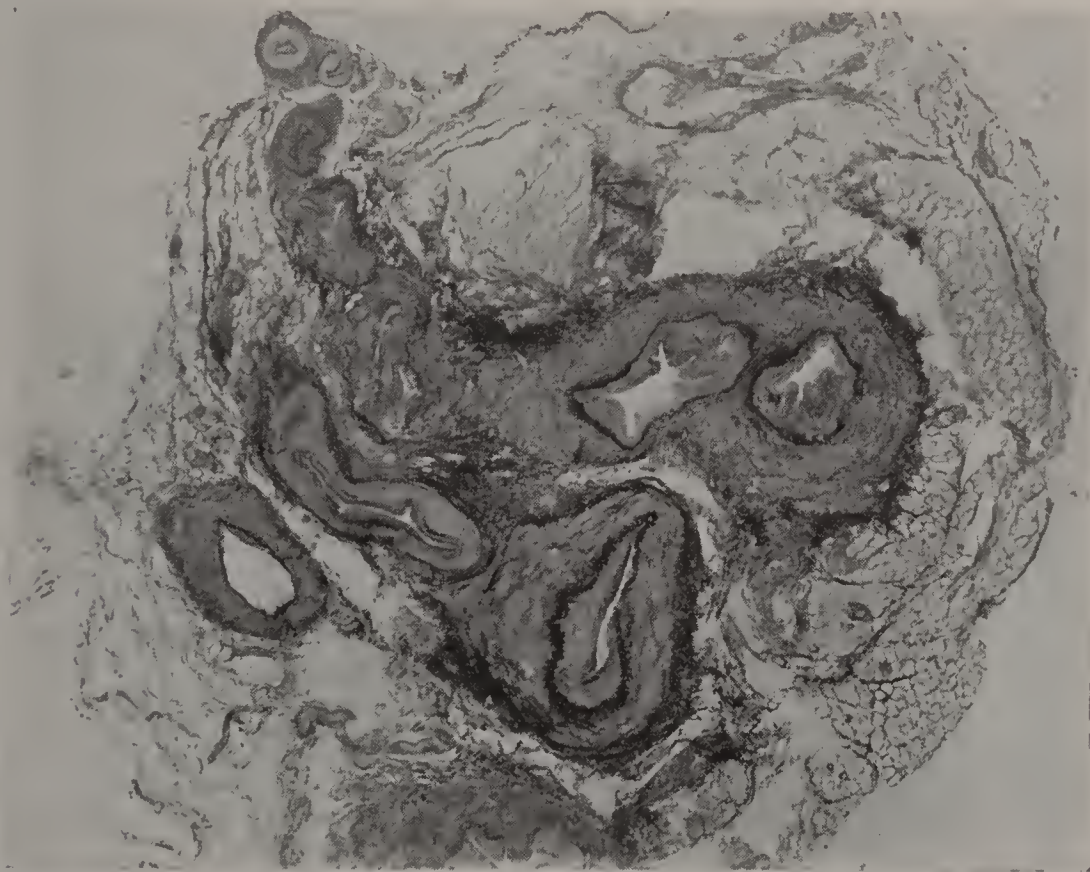


FIG. 126.—Fibrosis of perivascular tissues binding the two vessels above together; endarteritis and endophlebitis here simulated.

Of great value is a study of those sections that include a number of the larger obliterated vessels, as is seen in Figs. 125 and 126. Many of these will exemplify the secondary sclerotic intimal changes¹ that occur long after the occlusion has taken place; and further, they will demonstrate the fibrosis that binds the arteries and veins together, being the sequel of an inflammatory process extending from the adventitia. Fig. 126 shows beautifully how the two vessels on the right are encased in a dense fibrous sheath, whilst the large canalizing lumina suggests endarteritis obliterans rather than thrombo-angiitis obliterans. No wonder then that these lesions should so long have been misinterpreted.

CHAPTER LXIII

THROMBO-ANGIITIS OBLITERANS—PATHOLOGY IN LETHAL CASES

The autopsy material studies by the author was obtained from cases that died after amputation or from other causes. In the former, exitus was due either to pulmonary embolism, embolism of the mesenteric arteries, or to accidental causes.

Little is known regarding the participation of arteries other than those of the extremities in the characteristic process. The author has observed the "old type" of occlusion in the spermatic artery; and in a branch of the gastric artery leading to a callous ulcer of the stomach. Since but a small amount of material was at hand, it would be audacious to assert positively that the lesion was identical with that of thrombo-angiitis. However, recently the typical "acute" lesions were found in the spermatic vessels of the cord.

In a young man who consulted the author for a subacute enlargement of the testis, epididymis and cord, the diagnosis of tuberculosis or thrombosis of the vessels of the cord was made. Orchidectomy yielded an interesting specimen in which most of the veins (spermatic) of the cord and tributaries about the testis, were thrombosed. Microscopic examination revealed the typical "acute lesions" in many of the vessels.

The literature is practically devoid of reliable information on this point, so that autopsy material is highly desirable for enlightenment. But few data could be gathered since only 3 autopsies² were done on the cases under the author's observation. Great care must be exercised in interpreting the significance of the endarterial lesions evidenced by necropsy, since years had elapsed in 2 of the cases since the amputations of the lower extremities had been performed, during which time intercurrent affections, atherosclerosis and secondary thromboses could play a rôle in producing the final anatomical and pathological results. Because of the paucity of such records in the literature, however, it may be valuable to give in detail these findings, even though a final and authoritative interpretation of their importance and meaning may not be permissible from the meager data at hand.

¹ See also similar alterations in the veins.

² Autopsy material and findings in an additional case, in which the fatal outcome was accidental and due to hemorrhage in the wound were put at the author's disposal through the courtesy of the Pathological Laboratory, Mt. Sinai Hospital.

The fact that in the autopsy material at our disposal, the lesions of thrombo-angiitis obliterans were confined to the vessels of the extremities, might lead to much speculation and critical query. It would seem that local predisposing factors must needs be requisite for the special susceptibility of these vascular territories. In the present state of our knowledge we think it unwise to attempt to give explanations for all of the many seemingly inexplicable circumstances that surround this interesting malady. That the arterial channels affected by thrombo-angiitis become, or are inherently predisposed to atherosclerotic changes as well, seems proven both by autopsy material as well as through our studies of the amputated limbs. Where reamputation is done years after the more distal part of the limb has already been removed, more marked atherosclerosis is found. Or, when the second lower extremity requires amputation years after the first, atherosclerotic changes may be found that were absent during the earlier years of life; they may be slight or marked in degree.

The fatal termination in some of the cases may be accidental, dependent on the cardiovascular system, or may be preceded by a state of malnutrition and asthenia occasionally observed in cases of extensive atherosclerotic disease that have already lost both lower extremities.

The following grouping is now permissible in consonance with the author's experience: (1) the fatal cases in which death may be attributed to the operation, or some sequela of the disease itself (accidental); or (2) cases with asthenia and slow termination, possibly with cerebral arterial involvement.

1. Accidental Exitus.—As accidental we would designate the lethal outcome in cases that die from cardiac failure after operation, from hemorrhage or from pulmonary embolism. The author has personal records of but 2 cases of embolism with fatal termination after Gritti-Stokes amputation. In one there was pulmonary embolism with sudden exitus, in the other, mesenteric thrombosis or embolism. Cases collected elsewhere¹ afford instances of accidental complications and death, such as fatality from hemorrhage at the site of the ablation. In one such instance the autopsy material studied by the author again confirmed previous observations in the finding of atherosclerosis of some of the larger vessels and in the absence of the thrombo-angiitis process outside of the peripheral territories.

Case 1. Thrombo-angiitis; precocious atherosclerosis; coronary artery disease; sudden exitus.

F. K., male, aged 24, when admitted November 5, 1907, stated that 1 year ago he had severe pain in the left big toe; this recurred 2 weeks ago, and has grown progressively worse; the foot is swollen, red, and tender; for the past 2 days the big toe has become bluish in color; intermittent cramp-like pains in the calf of the right leg have also been experienced.

On physical examination the left foot is seen to be very edematous up to the ankle; tenderness of the big toe and cyanotic discoloration; slight erythromelia of the toes of the right foot.

Nov. 6, 1907, incision and drainage of cellulitis of left foot; Nov. 8, amputation of left big toe for gangrene; Dec. 19, *left dorsalis pedis pulse absent, right present*. Because of the failure on the part of the wound to heal, amputation at the left knee was resorted to, May 8, 1908.

Further examinations May 27, 1908, revealed *absence of right dorsalis pedis and posterior tibial beats*, and slight ischemia of the right foot upon elevation; July 15, still absent right dorsalis pedis and posterior tibial pulses, but good pulsation in the right popliteal artery; ulceration of the left stump; Aug. 20, absent left popliteal, only faint popliteal right, and pain in the right foot and calf.

On physical examination Jan. 23, 1909, there was marked erythromelia of the entire right foot, edema of the first and second toes, which were also in a state of trophic distur-

¹ Studied with the permission of Drs. Mandlebaum and Libman of the Pathological Department, Mt. Sinai Hospital, N. Y. C.

bance. March 1, 1909, amputation of the right leg at the middle third for impending gangrene.

The patient was lost sight of until May 2, 1911, when he returned to the hospital because of the presence of a painful sinus on the right stump which had persisted for 3 months. Both femoral pulses were good at this time, but *the right popliteal had completely disappeared*. Because of the pain and ulceration, Gritti-Stokes amputation of the right thigh was performed May 29, and, although the patient had engaged in conversation with the nurse following the operation, was shortly afterwards *found dead*.

Histologic examination of the vessels from the right and left legs established the diagnosis of thrombo-angiitis obliterans.

Autopsy Diagnosis: Thrombo-angiitis obliterans atherosclerosis of the coronary arteries, interstitial myocarditis.

Heart—Rather smaller than normal; tricuspid orifice about normal, tricuspid flaps show no thickening; right ventricle outflow tract dilated, wall very thin measuring about 2 to 9 mm. Pulmonary valves show no abnormality; few fatty plaques at the origin of the pulmonary artery; left auricle endocardium somewhat whitened; mitral valve shows distinct thickening at its edges; left ventricle dilated; heart muscle very brown, measures 8 mm. in thickness and throughout it yellowish areas of degeneration can be seen, some of which look fatty and other areas of a more or less circumscribed fibrosis. Such lesions can only be found in the wall of the left ventricle, and not in that of the right; left coronary artery is normal for about 1.5 cm. from its origin, when the main branch running down to supply the left ventricle is found to be more or less filled by fibrous, yellowish white substance, which is adherent to the wall and divides the lumen of the vessel into two very small parts (recanalization?). This fibrous process in the lumen of the vessel can be traced down for about 3 cm., when the vessel is lost. The right coronary artery and veins show no such change. At the point of origin of the right coronary artery there is an atherosclerotic plaque on the right posterior sinus of Valsalva, which encroaches upon the lumen of the orifice of the right coronary to such an extent as to very markedly obstruct it; in fact, the orifice is only pin-point in size. There are numerous pin-head and slightly larger atherosclerotic patches scattered diffusely beneath the intima.

Lungs—Both lungs show very dense adhesions at the apices and along the posterior border.

Liver—About normal in size, dark reddish brown in color.

Spleen—About one and a half times normal size, shows the presence of 2 depressions beneath the cortex, which on section are found to be healed infarcts, and consist of fibrous tissue containing some yellowish pigment; capsule slightly thickened and has a few adhesions scattered over it. On section, the organ is of a bright red color, very soft and the Malpighian bodies stand out prominently; splenic vessels show no changes.

Kidneys—About normal in size; capsules strip easily. The cortex shows a few smaller and larger reddish depressions, evidently healed infarcts. On section, the cortex and medulla of normal proportions, markings fairly distinct.

Microscopic examination of the coronary arteries presents the typical picture of arteriosclerosis. In short, marked lesions of atherosclerosis in the coronary arteries, but nowhere any evidences of thrombo-angiitis obliterans in the vessels examined.

Case 2. Thrombo-angiitis; extensive atherosclerosis; bland thrombosis in aorta, celiac axis, superior mesenteric arteries; exitus.

In the case B. D., aged 21, male, a typical Gritti-Stokes amputation of the left thigh was done July 19, 1916, and the usual lesions of thrombo-angiitis obliterans found in the vessels of the extremity, even at the site of ablation in the popliteal artery. July 21, the patient complained of intense pain in the abdomen, and there was marked rigidity of the abdominal wall. Per rectum a boggy mass could be felt, and the patient was in great distress because of the pain and distension. The diagnosis of mesenteric thrombosis was established, and at operation July 22, gangrenous gut was revealed; exitus.

Author's notes on viewing autopsy July 24, 1916: Extensive thrombosis of the celiac axis and of the superior mesenteric artery; gangrenous gut; the femoral artery and external iliac on the side of the amputation, about 1½ inches above Poupart's ligament thrombosed. In the external iliac there is a stagnation or accretion thrombus descending to meet the top of the old thrombus; in the femoral or possibly the distal part is an extension from the old clot in the femoral (accretion and stagnation).

In the aorta, mural thrombi some extending into the celiac axis and the superior mesenteric; numerous infarcts in the spleen, in the kidneys, and infarctions of the heart.

Autopsy July 22—Body is that of a young adult male; no icterus or petechiæ; moderate rigor mortis. Left leg has been amputated above knee; surgical incision through right rectus muscle.

Heart—on the anterior surface of the right auricle, near the base, milk-spot the size of a five cent piece; right heart moderately dilated; the tricuspid and pulmonary orifices normal; mitral shows few small yellowish, atheromatous patches. In the inner leaflet of the posterior wall of the outflow tract, near the aortic orifice, is an irregular, grayish patch which, upon section, appears to be diffuse scarring. Another similar patch is found in the muscularis near the apex. Coronary vessels show very marked atheroma; entire intima presents numerous raised patches. Here and there, however, are small button-like elevations due to nodules in the media of the vessels over which the intima appears perfectly normal.

Aorta—elasticity normal; entire intima studded with irregular, yellowish, atheromatous patches (ordinary atherosclerosis). In the upper part of the arch near the origin of the great vessels are two button-like patches, about 2 cm. in diameter. On section, these are situated in the media and consist of dense fibrous tissue, the intima and adventitia covering them not being involved. The fatty atheromatous changes in the intima extend all the way down the thoracic and abdominal aorta on its posterior wall, also on the posterior wall near the site of the celiac axis, is a thickening of the intima similar to that described in the aortic arch, which has apparently ulcerated into the lumen. The base of the ragged ulcer is covered by a layer of blood platelet thrombus. About 1 inch below this, also on the posterior wall of the vessel, is a still larger patch which is ulcerated. The base of the ulcer is also covered with blood platelet thrombus which extends down into the common iliac artery, occluding it completely at about $1\frac{1}{2}$ inches from the bifurcation. The left common iliac artery is closed by red thrombus. In the upper portions of the femoral artery, however, the thrombus again becomes blood platelet in type, and on the posterior wall of the femoral artery is a marked fibrous thickening, apparently disease of the vessel. The superior mesenteric artery is closed at the beginning by a blood platelet thrombus, lower down by a red thrombus. The mesenteric vein is filled with red thrombus. One of the main branches of the splenic artery is also filled with a blood platelet thrombus.

Liver—moderately enlarged, cloudy parenchyma.

Spleen—about $1\frac{1}{2}$ times its normal size; center portion presents a large, firm, yellowish, anemic infarct similar to the infarct seen in subacute bacterial endocarditis.

Kidneys—normal in size, capsules strip with some difficulty, surface smooth; intense congestion of the parenchyma.

Adrenals and pancreas—negative.

Gastro-intestinal tract—intense congestion of the serosa of the stomach and small intestines; complete gangrene of the terminal 4 feet of ilium.

Microscopic examination of the superior mesenteric, common iliac, femoral, external iliac, abdominal and thoracic aorta showed the typical lesions of arteriosclerosis with varying degrees of thrombosis (parietal and occlusive) of the mechanical type; nowhere lesions of thrombo-angiitis obliterans.

2. Cases with Slow Termination.—Just as in certain cases extensive aortic thrombosis was found, so here the mental condition antedating exitus would suggest the possibility of thrombosis of bland or specific (thrombo-angiitis) type in the territory of the cerebral vessels. Such a case is the following.

Case 3. Amputation of both lower extremities and one upper; duration of disease 10 years; exitus with cerebral symptoms.

S. A., aged 35, male (see Chapter on Thrombo-angiitis Obliterans of the Upper Extremities), when examined August 11, 1903, reported trouble in the left foot, 3 years previously. Since then there were attacks of pain in both feet.

For the past 2 days (Aug. 11) the left foot has been painful, particularly at night, so that now he is unable to stand. His clinical course may be divided into four stages; (1) gangrene of the left leg; (2) gangrene of the right leg; (3) gangrene of the left forearm; and (4) cerebral symptoms leading gradually to exitus.

1. Amputation of the Left Leg.—Examination reveals early signs of gangrene of the great toe of the left foot. Aug. 11, 1903, amputation of left leg; Aug. 15 to Sept. 2, no tendency to heal, sloughing marked; Sept. 5, reamputation through the knee; Sept. 22, again necrosis of the flaps; Oct. 3, reamputation through the middle of the thigh. A thrombus 4 inches in length was extracted from the femoral artery; Oct. 24, wound healed.

2. *Amputation of the Right Leg*.—March 23, 1905, says he has been suffering for 8 weeks with pain in the right foot. An ulcer developed on the inner side of the heel, and recently this region has become black.

Examination reveals a gangrenous area over the right heel; March 31, 1905, amputation through the upper third of the right leg; March 15, 1907, because of recurrence of gangrene in right stump, reamputation through lower third of thigh; June 13, 1907, patient insists upon leaving hospital, although bare bone with suppurating sinuses can be still detected.

3. *Amputation of Left Forearm*.—March, 1910, says that since 6 weeks has had severe pain in index and middle fingers, which gradually became swollen and red; after the incision of a bleb at the tip of the index finger, gangrene of index and middle fingers set in. Notes made March 14, 1907, called attention to the absence of the left radial pulse and cyanosis of the hand. March, 1910, amputation through forearm for gangrene.

4. *Exitus with Cerebral Symptoms*.—April 14, 1914, patient admitted to hospital in stuporous condition. There had been no apoplexy and no signs of palsy. Physical examination—patient incoherent in speech; talks in mumbling unintelligible manner; pupils are equal and react to light; right upper lid is ptosed; right radial pulse absent (the left forearm has been amputated); left thigh stump contains a sinus; from the right stump dead bone protrudes; April 24, 1914, condition unchanged; April 29, temporal pulse weak; marked asthenia; exitus.

Case 4. Amputation of both lower extremities for thrombo-angiitis obliterans; obliteration of the brachial arteries with a clinical semblance of scleroderma and sclerodactyly, lethal outcome, autopsy showing thrombosis of a portion of the aorta.

I. L., male, aged 35 years, examined Oct. 3, 1906, said he had always been well. Ten months ago he began to experience pain in the left ankle shooting into the toes (acute stage of the disease in the deep vessels, plantars and posterior tibial behind the ankle?). At first this was intermittent but soon became constant. He became progressively worse so that he was then confined to his bed for several months because of the pain. He was in the hospital a few months previously when amputation was suggested, which was refused. About 1 month ago the toes of the left foot became dark in color, exceedingly painful and then an ulcer developed on the dorsum.

Physical examination: A rather poorly nourished man; good radial pulsations. The left foot is the seat of gangrene involving the second toe, which is black. The other toes are deeply cyanotic, partly anesthetic. Near the root of the second toe on the dorsum there is a sloughing ulcer the size of a quarter, at whose base a tendon is exposed. The dorsalis pedis pulse is absent. Lymphangitis extends upwards to the mid-calf. The popliteal and femoral arteries pulsate.

Oct. 3, 1906, osteoplastic amputation of the left leg through the mid-calf region. Necrosis of the flaps and bone, with healing, Nov. 17, after removal of dead bone and sloughing skin.

Pathological examination of the occluded vessels showed the typical lesions of thrombo-angiitis obliterans.

In June, 1907, the pain in the *right leg* became so intense, that although gangrene had not occurred, the patient begged for amputation of this leg too. Therefore, July 1, 1907, an osteoplastic amputation was done, but because of unsatisfactory healing reamputation had to be resorted to, July 15, 1907.

Pathological examination of the obliterated arteries showed both the *old* and *acute* lesions of thrombo-angiitis obliterans. The posterior tibial contained miliary giant cell foci characteristic of the disease.

Dec., 1909. The patient says that he had a "sore" on the outer surface of the left stump about 1 year ago. He had no pain in the stump until 1 year ago, when a painful wound developed that took 3 months to heal. Three months ago pain in the right stump set in; at the tip a sore developed which refused to heal, and became gradually worse.

Physical examination, Dec. 15, 1909: This reveals swelling of the entire right stump. Posteriorly in the flap there is an ulcer the size of a dollar with gangrenous margin. The whole stump up to the upper border of the patella is discolored; has a purplish reddish hue. In the elevated position there is a fair amount of ischemia. The left stump shows marked erythromelia, otherwise negative. Both femorals and popliteals fail to pulsate.

On December 17, 1909, the patient stated that he had had trouble with his *right hand* for several months. He has noticed "swellings" along the front and inner aspects of the arm, forearm and hand. The use of his hand has become impaired, the hand has become *thinner*, and the skin relatively *thicker and dryer*.

On physical examination of the right hand it is seen that all the fingers look like those of *sclerodactyly*; *movement* of the distal joints is diminished. The skin is atrophic, dry, and the circumference of each finger is considerably less than that of the fingers of the left hand.

No radial or brachial pulse is palpable; the brachial artery can be felt as a hard cord. An axillary pulse can be obtained.

Examination of the vessels of the left hand reveals absent radial and ulnar pulsations, fairly good brachial pulse. There are no trophic disturbances.

Neither femoral pulse is obtainable.

X-ray examination of the hands, Dec. 23, 1909, shows *atrophy of all the bones*.

The patient was readmitted to the hospital April 11, 1911, complaining of pain in the left stump; the condition of the hands unimproved.

April 26, reamputation of the left stump for ulceration and sloughing. The femoral artery and vein were found occluded. May 2, skin flaps blue and poorly nourished; May 5, no union of external half of wound, union of inner half incomplete, tissues appear necrotic. May 25, during the past few days the patient has become more lethargic; temperature ranges from 100 to 102.5°; tongue dry, cracked; patient unable to answer questions, drowsy; left stump necrotic; May 30, patient considerably weaker and comatose, exitus.

Autopsy Diagnosis: Thrombo-angiitis Obliterans, Thrombosis of Abdominal Aorta.—General—body is that of a rather emaciated man, marked rigor mortis, both lower limbs amputated through the thighs.

Heart—rather smaller than normal; subpericardial fat slightly increased in amount. Tricuspid valve admits 4 fingers, and tricuspid flaps are normal. Right ventricle is widely dilated; muscle quite brownish and extremely thin. Some invasion of the muscle by subpericardial fat. Pulmonary valve shows no abnormality; no signs of atherosclerosis in the pulmonary artery; left ventricle endocardium somewhat whitened. Mitral orifice admits 3 fingers easily; mitral flaps very slightly thickened; left ventricular muscle brown and of about normal thickness; avenue of outflow widely thickened. Aortic valve shows slight fenestration and thickening of the corpora Arantii, corresponding to about the third degree of atherosclerotic process.

The aorta elasticity is normal; a few, small, fatty areas in the intima around the orifice of the anterior coronary artery; a few very slight fatty plaques in the intima of both coronaries.

Aorta—from the arch down to the level of the superior mesenteric is of normal thickness and elasticity, and shows only a very few, small, yellow, fatty areas in the intima. The vertebral branches come off regularly. The coeliac axis and its branches show not the slightest thickening, similarly with the superior mesenteric, but beginning just below the origin of the latter, is a fusiform expansion of the aorta about 3 cm. long, 2.5 cm. wide and 2 cm. thick. Below this the nature of its continuation is doubtful because the aorta has been torn off just above the bifurcation, but, although the swelling tapers downward, it probably was continued into the iliacs.

Around the swelling of the aorta is dense fibrous tissue (periarteritis). On cutting through the center of the fusiform swelling the aorta is found to be filled with a mass of what appears to be organizing thrombus. The vessel wall itself appears even thinner than normally. The mass of tissue in the lumen is firmly adherent to the wall of the vessel. The part on the periphery of the mass and immediately adjacent to the intima is firm and yellowish in color, whereas the central part is of a cherry red color and much softer. Just to one side of the center the material is a deep red, very soft and resembles more closely rather fresh clot. When the aorta is opened down to the beginning of this process and when the mass within the lumen is viewed from above downward it is seen to begin 0.5 cm. below the origin of the superior mesenteric artery, here being entirely parietal and adherent to the intima of the anterior half of the vessel wall. The vessel is completely closed about 2 cm. below the origin of the superior mesenteric artery, but as has just been said, it sends up a parietal tongue-like process which is adherent to the anterior half of the wall. This tongue-like process is of a deep pink color, firm in consistency and densely adherent to the vessel. The two renal arteries are given off above the level where the aorta is completely occluded, and from the portion of the aorta which contains the parietal mass. The left renal appears normal and is perfectly free of clot, but the right renal contains at least for 7 mm. from the point of origin (which is all the vessel that is on the specimen), a parietal mass which is firm in consistency, pinkish grey in color, semi-translucent. It is about 1 mm. in thickness, and runs completely around the entire circumference of the vessel, narrowing the lumen to a diameter of 2 mm.

Liver, pancreas and intestines negative.

Right kidney—shows evidence of parenchymatous degeneration, striations poorly marked. Renal artery and vein show no changes whatever.

Left kidney—cortex about $\frac{1}{2}$ normal thickness and the markings extremely faint; peripelvic fat increased in amount. Near the upper pole of the organ and situated about 0.5 cm. beneath the surface is a multilocular cavity containing greenish pus, the walls of which are smooth and consist of fibrous tissue, in some places being 2 mm. thick.

Microscopic Examination.—This showed none of the typical lesions of thrombo-angiitis obliterans in the aorta or renal vessels. The lesions were those of *recent thrombosis with bland type of organization and arteriosclerosis*.

CHAPTER LXIV

THROMBO-ANGIITIS OBLITERANS—DIAGNOSIS

Much to the confusion of our diagnostic concepts of the circulatory affections, individual and combinations of manifestations loom up and enter into the clinical field under extremely varied disguises.

Thus, pain on walking may be associated with blanching of the feet; or, spontaneous vasomotor ischemia may be followed by rubor and cyanosis—both types occurring in thrombo-angiitis obliterans, and mimicking Raynaud's disease.

Chronic rubor and pain, a combination common in thrombo-angiitis obliterans and atherosclerotic vascular occlusion may simulate erythromelalgia.

The chronic atrophies and the indurated skin sometimes accompanying advanced lesions of thrombo-angiitis obliterans may be mistaken for scleroderma and sclerodactyly.

The transmutations and kaleidoscopic nature of the dominant features of thrombo-angiitis are in singular contrast with the more stable clinical symptoms of the vasomotor neuroses.

Thrombo-angiitis obliterans must be diagnosticated from, *first*, lesions of other organic vascular diseases of the extremities, *second*, cases of neuropathic or neurogenic vascular disorder of the extremities. In the first group belong athero- and arteriosclerotic gangrene, endarteritis obliterans, embolic and thrombotic gangrene. In the second group belong Raynaud's disease, erythromelalgia, acro-paresthesia, multiple neurotic gangrene, scleroderma, sclerodactyly, and chronic acro-asphyxia. A careful clinical study of thrombo-angiitis obliterans will dissipate all doubt as to the possibility of separating this disease, as a clinical entity, from the other types of organic vascular disease, as well as from all those neurogenic varieties of vasomotor and trophic disorders that may be clinically confounded with it.

Characteristic for thrombo-angiitis obliterans are the following groups of symptoms: (1) the disappearance of the pulses, particularly the dorsalis pedis, posterior tibial, and popliteal, more rarely the femoral, radial and ulnar; (2) the development of typical manifestations of impaired circulation, to wit: Blanching of the lower extremities when these are elevated above the horizontal, hyperemia (rubor or erythromelia) or reddening of the foot in the dependent position during certain stages of the disease, and trophic disturbances, such as impaired growth of the toe nails, slightly atrophic condition of the skin, ulcers, and gangrene; (3) true vasomotor phenomena of transitory nature, such as alternating syncope, rubor, coldness apparently independent of those chronic changes that have been cited above, and that are distinctly traceable to the occluded condition of the arteries and veins; (4) the symptoms of pain, either in the form of intermittent claudication (pain in the calf of the leg or in the foot on walking with cessation when the limb is at

rest) or the severe pain that is associated with the advent of trophic disturbances, especially with ulcers and patches of gangrene; (5) the slow course of the disease, symptoms of intermittent claudication or pain, preceding the development of trophic disturbances for months and years; (6) the fact that about 99 per cent of the cases occur in Polish, Galician or Russian Hebrews, and that almost always young males between the ages of twenty and thirty are taken with this disease; (7) the onset of symptoms in the lower extremities, one of the legs being first affected; (8) the comparative infrequency of involvement of the upper extremities; (9) the association of a peculiar type of migrating phlebitis in the territory of the external or internal saphenous, less frequently in the larger veins of the upper extremities, characteristic in about 20 per cent of the cases; (10) the slow but steadily progressive course, leading in a large majority of the cases to amputation of at least one limb, not infrequently of both lower extremities, and in rarer instances to amputation of one of the upper extremities as well.

For the *clinical diagnosis of thrombo-angiitis* we must depend upon (1) the racial (Hebrew) and sex (male) predilection; (2) the early involvement of the lower extremities; (3) the early symptoms of pain or intermittent claudication; (4) the presence of migrating phlebitis; (5) the evidence of pulseless vessels; (6) the presence of blanching of the extremity in the elevated position; (7) the existence of rubor in the dependent position; (8) the relation of the hyperemic phenomena to posture; (9) the absence of simultaneous, symmetrical involvement; and (10) the slow, progressive chronic course terminating in gangrene.

Differential diagnosis between thrombo-angiitis obliterans and the vasomotor neuroses: Were it not for the fact that certain symptoms, closely resembling typical vasomotor phenomena, may persist for weeks and years in this disease, confusion with the true neurogenic vasomotor process would scarcely ever arise. The chronic condition of redness in thrombo-angiitis obliterans can be explained as due to dilatation of the superficial capillaries, this being a compensatory phenomenon making for an adjustment of the impaired circulation. This chronic redness or rubor may be mistaken for erythromelalgia, or for the rubor of Raynaud's disease. The fact that it is associated with other evidences of closed vessels and the other characteristic features above mentioned, together with the circumstance that the redness disappears at once upon elevating the extremity, will make the recognition of its nature possible.

For the recognition of thrombo-angiitis of the upper extremities, it is well to separate the cases in which vasomotor symptoms predominate, from those in which the symptoms in the lower extremities are well marked; and also, to distinguish those in which we are compelled to investigate very carefully in order to elicit evidences of vascular occlusion.

The symptoms simulating Raynaud's disease and acro-asphyxia are cyanosis of the finger tips, coldness of the fingers with or without trophic disturbances, and alternating cyanosis and rubor, involving the fingers or the whole hand. Rather characteristic in the symptomatology of thrombo-angiitis is the apparent dependency of the vasomotor symptoms upon variations in temperature, the chronicity of the manifestations, the absence of pain in some of the cases, and the absence of paroxysmal nature of the attacks so characteristic in Raynaud's disease.

When we turn to those patients in whom the trophic disturbances seem to be unassociated with evidence of vasoconstriction and vasodilatation we note that there is merely a history of the development of a spontaneous ulcer of the

fingers. It seems more than likely that in many of these the history of the absence of the vasomotor phenomena would be found unreliable if it were possible to observe the cases throughout the whole course of the disease. Future observations will probably support my belief that here, too, some manifestations of deranged vasomotility do occur.

When we consider the largest group, namely, that in which gangrene of small or greater extent develops, we find that some cases may be mistaken for simple paronychia. Others claim that the development of a gangrenous patch or of the felon was preceded for a long time by distressing pains in the tips of one or more fingers. The vasomotor symptoms may be absent or the cyanosis and redness may be quite striking. The following sequence of symptoms may be observed and is interesting, because pain and trophic disturbances alone are complained of. The onset is marked by severe pain in the tip of a finger. This is superseded by atrophic changes in the skin, the development of a dry, hard patch, mortification, and also formation of an ulcer. In still other cases the similarity with Raynaud's disease is even more marked, for the symptoms are pain, cyanosis, rapidly followed by gangrene.

More rarely do we meet with those interesting examples of the effects of arterial occlusion in which the development of intense atrophy of a hand or limb or the production of the typical picture of scleroderma and sclerodactyly is the significant feature of the clinical picture.

The differential diagnosis of this condition from the *vasomotor neuroses* may however be difficult in the cases in which we cannot exclude the association of the two diseases. It will be noted that where coldness and cyanosis are complained of, a distinct dependency on temperature or other environmental condition can often be elicited or that pain is absent. The presence of vessel changes and the history of the involvement of a lower extremity at once clear up the diagnosis.

Where trophic changes alone are present, the absence of symptoms referable to the central nervous system speaks decidedly against nerve lesions. The relation of the vasomotor symptoms to the position of the limb will in other cases be of value in explaining the nature of the symptoms.

How can we explain the occurrence of true vasomotor phenomena such as do not seem to owe their existence to the mechanical effects of impaired circulation? The blanched appearance that is a sequence of an obstructive condition of the arteries, and which can be demonstrated by elevation of the leg, and in bad cases can even be elicited in the horizontal position, is a phenomenon easily explicable on the theory that the avenues of arterial supply are cut off through extensive obturation of the arteries. Many clinical and experimental observations have been gathered that speak in favor of this view. So also is the rubor not a true vasomotor phenomenon, but a sign of chronic vasodilatation of the superficial capillaries and is compensatory in nature. The part played by the vasomotor mechanism in its production is discussed in Chap. XLVI.

On the other hand, veritable symptoms of *disturbed vasomotility can be associated with thrombo-angiitis obliterans*. That these should occur is not surprising when we call to mind that not only have intense and extensive destructive, pathological alterations taken place in the most important arteries of a limb, but that the accompanying nerves are frequently bound down by a dense mass of cicatricial tissue and have undergone severe fibrotic changes. Although the mechanism of the irritative and exhaustive vasomotor phenomena is not clear, the total disorganization of the vascular innervation in many of the cases would seem to afford some basis for the possibility of the

occurrence of the disturbances which we call "vasomotor" in nature. Other theories are discussed elsewhere.¹

Where signs of thrombo-angiitis of the lower extremities are unquestionably present, and where evidences of vascular occlusion in the upper extremities are lacking, although these are the site of disturbed vasomotor innervation, we may for a long time be unable to rule out the possibility of the simultaneous occurrence of two different diseases.

In addition to this more or less chronic or permanent sign of deranged circulatory function in thrombo-angiitis other phenomena which are truly vasomotor in nature may frequently be associated; and, it is these that must be differentiated from similar phenomena accompanying Raynaud's disease, erythromelalgia, scleroderma, sclerodactyly, and acrocyanosis.

In order that a differential diagnosis may be clearly presented, let us briefly recapitulate the typical course of a case of *Raynaud's* disease. The latter is an affection whose pathology has not as yet been definitely determined, the lesion doubtlessly residing somewhere in the central nervous system. Its clinical characteristics may thus be summed up: Somewhere in the peripheral portions of the body (so-called acra) there occurs more or less severe pain not confined to distinct nerve territory, usually affecting symmetrical parts, attacks of vasomotor disturbance being part of the syndrome. These latter are (1) syncope, asphyxia, or local rubor, and (2) severe trophic disturbances, usually in the form of gangrene of the parts first affected with symptoms. The course is an intermittent one, for there may be completely free intervals; but in some instances, evidences of disturbed vasomotility may persist. The disease may consume itself in one attack or several attacks may occur in succession. Objectively, sensory disturbances are usually absent, as well as paralysis, although other evidences of disturbed vasomotor innervation, such as aphasia, hemoglobinuria, arthropathy, may occur. Usually neuropathic individuals are affected. The organic vascular changes, as well as the lesions of the nervous system, reported as occurring in some of the cases, have doubtless no causative relation with the disease.

It is true that there are still some who cling tenaciously to the theory that some lesions of the peripheral arteries may account for the symptoms of Raynaud's disease. In support of this view, certain anatomical findings have been cited as strong arguments by those who believe that a definite anatomical lesion in the peripheral vessels is irresistible testimony against pure hypothesis. A careful analysis of the cases in question, as made by *Cassirer*, shows that reported organic alterations in the vessels will not suffice to explain the symptoms any more satisfactorily than the theory of a central nerve affection of the sympathetic system. Whereas in thrombo-angiitis obliterans the territory manifesting symptoms, corresponds to that containing the diseased vessels, we find that no such relation exists where vascular lesions are associated with Raynaud's disease.

In *Raynaud's* disease we will note the following features: A sudden onset of the first stage of local syncope or regionary ischemia involving usually the fingers, more rarely the toes, and occasionally the margins of the ears or the tip of the nose with coldness and blanching; associated sensory phenomena, paresthesia, and pain; a comparatively short duration of the vasomotor and sensory manifestations, their intermittent character with return to normal between the attacks; the symptoms of local asphyxia attended with local depression of temperature and swelling of the parts involved; the disappearance

¹ Chap. LXXXVI, also Chap. LIV.

of the asphyxia with substitution of reactive hyperemia and a third stage of dry gangrene. Characteristic for this disease as well as for the cases of scleroderma and sclerodactyly is the striking atrophy of the ends of the distal phalanges. The changes in the bones can be well demonstrated by Roentgen-ray examination, atrophy and disappearance of large portions of the end-phalanges being distinctive and diagnostic features. In our own experience the alterations in the bones could be detected early in the disease, probably developing simultaneously with the other trophic disturbances.

The differentiation of true scleroderma from thrombo-angiitis will be rarely difficult to make. In scleroderma and sclerodactyly the first stage with hard edema is characteristic and never simulated by cases of organic vascular disease. The second indurative stage may, however, be almost exactly reproduced by other affections. The form of scleroderma known as "sclerodactyly" because of attendant alterations in the deeper tissues, may not be unlike thrombo-angiitis. Roentgen-ray examination of the hand in sclerodactyly offers the most valuable means of differentiating the two diseases. The phalanges will very early show atrophic changes and disappearance of the terminal portions in scleroderma, sclerodactyly, and Raynaud's disease, while the bones, although somewhat rarefied, will be seen to conserve their outlines throughout the course of the disease, thrombo-angiitis obliterans, until they are disturbed by the effects of gangrene.

So far as our experience permits us to judge, symptoms of scleroderma occur only late in thrombo-angiitis when other signs of vascular occlusion have already become well developed. The recognition of the condition will then depend upon the absence of pulsation in the larger peripheral vessels, the presence of gangrene (or the history of such a condition) and of the other typical signs of obliterated arteries and veins.

It is most probable that in Raynaud's disease and the related affections the seat of the pathological process is to be sought in the vegetative system, that is, somewhere in the vasomotor apparatus. Nor are we likely to be rewarded in a search for any organic change. The frequent return to a normal condition, observed clinically, also speaks against the likelihood of morphological or chemical alterations in the nervous system.

Whereas in thrombo-angiitis obliterans a definite and specific morphological change in the arteries and veins is responsible for the varied phenomena in the superficial capillaries, in Raynaud's and allied diseases, the vasomotor and trophic disturbances are the outcome of irritative and exhaustive processes of the sympathetic nervous system.

CHAPTER LXV

THROMBO-ANGIITIS OBLITERANS—TREATMENT

It must be remembered that we have as yet no treatment for the *acute stage* of the disease in the sense of a procedure that has specific effect on the acute inflammatory process in the arterial and venous walls. Nor have we any prophylaxis against the disease. Whether salvarsan injections or drugs of similar action or other bactericidal agents may be of value, we cannot as yet determine, in view of a too limited experience. Certain it is, that when

we speak of treatment of the disease, we are in truth referring to therapeusis of the consequences of the "healed stage" and not of the morbid process per se. With this qualification, therefore, we may proceed to the discussion of what is known regarding the care of the many effects of the resultant impaired circulation.

The treatment should vary according to the stage of the disease, the presence of migrating phlebitis, trophic disorders and gangrene. Since the methods recommended for atherosclerotic cases often apply here, it is well to read the two chapters in this connection.

PROPHYLACTIC TREATMENT

If we accept the theory that the process is one induced by some infectious agent in arteries that exhibit a certain predisposition to disease, it is quite evident along what avenues future investigations of preventive nature should be directed. In all susceptible individuals then (racial proclivity, etc.) both the predisposing forces and the inroads of the specific type of noxious agent are subjects of concern.

To combat the former, all the usual stresses of mechanical or chemical nature that produce arterial inferiority (excessive exercise, exposure, certain foods, tobacco, etc.) must be avoided. As for the latter, however, we are still at a loss for either a preventive serum or medicament.

It would not be paradoxical to state that the only efficacious treatment of this disease is one of *pure prophylaxis*. For even with the most careful scrutiny and search for evidences of arterial involvement, we are usually unable to recognize the existence of the disease before arteries and veins over considerable territory are already irremediably damaged. It is perhaps only in those cases where a period of migrating phlebitis ushers in the malady and precedes the involvement of the deep vessels by months or years, that there is given us a period during which experimental work of preventive therapeutic nature can be applied.

As soon as signs of obstructive vascular lesions are diagnosticated, even before the advent of destructive alterations in the peripheral tissues, great stress should be laid on the importance of diminishing the functional demands on the local circulation. The agencies that are likely to disturb the fine balance between the tissue requirements and the permanently defective circulation, are the following: Prolonged standing, walking, compressing forces that produce local anemia, such as tight shoes, bands, etc.; exposure to cold with its sequence—ischemia of the parts (or to cold and moisture); mechanical insults that produce clean wounds or infections and thus call forth the need of an enhanced circulatory activity. In short, the locomotor apparatus must be spared as much as possible for its adaptive or accommodative powers are greatly reduced in this condition.

Treatment of Pain.—Clinical experiments have been carried out by the author and others with a view to blocking the afferent nerve paths. The Foerster posterior root section¹ has not found acceptance because of the magnitude of the operation. Silbert² recently reports complete relief of pain in 3 cases after the injection of absolute alcohol, care being exercised not to infiltrate adjacent tissues. Anesthesia of the sole of the foot with relief of pain is said to result immediately. Because of the occurrence of

¹ Elsberg, Case observed by author.

² Silbert, Jour. Am. Med. Assn., Nov. 18, 1922, 79, 1765

late palsies and trophic ulcerations the author does not recommend this method.

II. CONSERVATIVE TREATMENT

When the disease is well developed, distinct intermittent claudication being present and fairly marked pain with or without trophic disorders, it is advisable that the patient remain in bed for several weeks or even longer, or at least that walking and standing be completely interdicted. Therapeutic measures should be directed towards the conservation of warmth, enhancement of the circulation, the prevention of traumatism, and the treatment of local conditions, trophic disorders or gangrene, when these supervene.

A. Methods of Enhancing the Circulation. 1. *The Postural Method.*—The author has suggested that certain passive exercises may be of value in inducing hyperemia or rubor in the affected limb, and therefore, therapeutically beneficial in increasing the blood supply.

This method is the logical therapeutic outcome of the author's method of diagnosing impairment of circulation of the lower extremities, in that it uses the phenomenon of *induced rubor*, or *induced hyperemia* in a therapeutic way. If the method be carried out daily for a sufficiently long period, it is of greater value in improving the circulatory conditions and in increasing the blood supply, than any of the other mechanical or thermal means that are at our disposal.

The procedure is as follows: The affected limb is elevated with the patient lying in bed, to from 60° or 90° above the horizontal, being allowed to rest upon a support for from 30 seconds to 3 minutes, the period of time being the *minimum* amount of time necessary to produce blanching or ischemia. As soon as blanching is established, the patient allows the foot to hang down over the edge of the bed for from 2 to 5 minutes, until reactionary hyperemia or rubor sets in, the total period of time being about 1 minute longer than that necessary to establish a good red color. The limb is then placed in the horizontal position for about 3 to 5 minutes, during which time an electric heating pad or a hot water bag is applied, care being taken to prevent the occurrence of a burn. The placing of the limb in these three successive positions constitutes a cycle, the duration of which is usually from 6 to 10 minutes. These cycles are repeated over a period of about one hour, some 6 to 7 cycles constituting a séance.

The number of séances cannot be categorically stated but should vary with the case. In a general way they should occupy at least 6 to 7 hours a day, that is every alternate hour during the daytime. During the hours of rest, heat is applied continuously in the form of an electric pad, hot water bag, hot air apparatus, or electric lamp.

In the opinion of the author, this method does far more to improve the circulation than either the application of superheated air (so-called baking treatment), or the diathermic treatment.

The length of time of its application may require modification according to the manner in which the procedure is borne. In some cases pain induced by elevation may necessitate a diminution in the period of elevation.

It is not possible to lay down hard and fast rules as to the exact application of this method in any given case. Its employment should be varied according to the requirement of each and every clinical stage, and the patient's response. A more detailed discussion will be found in the chapter on Arterio-sclerotic Gangrene.

2. *Heat*.—For the cases of thrombo-angiitis obliterans, as well as arteriosclerosis, it is best to exclude the foot from the hot air treatment, when it is the seat of trophic disorders or gangrene. Heat may be applied either by means of an electric thermophore, by a hot-air apparatus, or an incandescent apparatus containing one or more incandescent lamps, or a single strong electric lamp with reflector. The temperature should not be raised higher than 120° F. at the first treatment, and gradually increased to 150° and 180° , but never more than 200° F. Heat is applied as high as the middle of the thigh, for about one-half hour. In the presence of migrating phlebitis this treatment is not well borne. Whenever gangrene is present, the gangrenous part is left covered with a dressing but not included in the apparatus.

The frequency of the heat treatments is to be varied in accordance with the reaction and the exact condition of the affected limb. It cannot be emphasized too strongly, however, that occasional applications (once or even twice in 24 hours) are of little therapeutic value, and that treatment over prolonged periods of time is necessary to obtain beneficial results.

3. *Diathermic Treatment*.—This is an excellent method of obtaining the effects of heat upon the deeper parts, and is particularly applicable to the early cases, especially those in which intermittent claudication is the most marked symptom, and in those patients in whom ambulatory treatment must be carried out. In the presence of inflammation, migrating phlebitis, ulcers or gangrene, it does not seem to be well borne or beneficial. The séances should last from twenty to twenty-five minutes.

The patient will feel the development of the heat in the region of the ankle, where the effects of warmth can be demonstrated by the touch. Subjectively, there is in addition to the feeling of heat, a dull ache which should not be allowed to become marked. Pain is a sign for diminishing the strength of the current.

Some authors claim success in the treatment of thrombo-angiitis obliterans by the diathermic method, which H. Wolf employs as follows.

The patient sits on a chair with each foot in a basin of warm salt water. Each basin is connected with one of the poles of the diathermic apparatus. This can be done simply by putting an electrical plate electrode with connecting wires into the water. The current is then turned on and increased according to the sensation of the patient, usually to about 700 M.A. The patient is allowed to increase and decrease the amount of current at will, so as to avoid excessive current strength. If it is desired to concentrate the current in the toes, a block of wood is placed under the heel so that it stands above the water. The current is then forced through the toes mainly, and the effect is stronger. The duration of treatment is from 25 to 30 minutes. The frequency depends upon the reaction. With the occurrence of inflammation or phlebitis, the treatment is discontinued. After subsidence of such complications, the treatment may be resumed and given daily.

4. Many attempts have been made to improve the circulation through the *subcutaneous or intravenous injection* of solutions that might diminish the viscosity of the blood. So Koga¹ employed Ringer's solution. Ginsberg² and Steel³ have suggested sodium citrate intravenously. Others (Meyer⁴) have claimed beneficial results after flushing the intestinal tract daily with

¹ Koga, Deut. Zeitschr. f. Chir., 1913, p. 371.

² Ginsberg, Am. Jour. Med. Sc., (Sept.), 1917, 154, 320.

³ Steel, Jour. Am. Med. Assn. (Feb. 12), 1921, 76, 429.

⁴ Meyer, Jour. Am. Med. Assn. (Oct. 19), 1918, 1268.

8 to 10 quarts of Ringer's solution through a duodenal tube, this supplemented by several daily subcutaneous injections of this solution. The belief that beneficial results follow intravenous administration of sodium citrate solution seems hardly warranted.

5. *Intermittent Compression of the Main Arteries.*—An exceedingly tedious but sometimes valuable method of inducing reactionary rubor and furthering the development of collateral circulation is intermittent compression or digital obliteration of the brachial or femoral arteries, when these are patent. The circulation in these vessels is made to cease by pressure of one or more fingers; the brachial artery being easily accessible at its beginning, the femoral just below Poupart's ligament. Where the facilities are at hand, the artery may be controlled for one minute and the circulation allowed to return for five minutes, this being repeated over a period of an hour. Such séances should alternate with those of the postural method and hot air treatment.¹

B. Internal Medication.—Mercury may be given in some cases in smaller injections when syphilis is suspected, although it does not seem to have any material effect upon the disease. Nitro-glycerin and iodides may be administered under certain circumstances, although their effects are of questionable value.

C. Local Treatment.—Trophic ulcers must be treated on general surgical principles, the combatting of the severe pain attending these being the most difficult part of the treatment. An ointment containing 5 per cent novocain, and 10 per cent orthoform or anesthesin in lanolin and glycerin is sometimes beneficial in allaying local pain due to trophic disorders. The continuous saline bath or repeated baths alternating with the postural exercises is a valuable adjuvant in aiding healing.

III. OPERATIVE TREATMENT

Ligation of the Femoral Vein.—Lilienthal has suggested the ligation of the femoral vein as of some value in enhancing the circulation. He claims that in some cases of sudden gangrene healing may take place after conservative treatment, such as removal of a toe alone, and that frequently a lower amputation will be more apt to be successful after ligation of a vein. The author cannot subscribe to this view.

Arteriovenous Anastomosis.—This has been suggested by Wieting with a view to reversing the circulation, the femoral artery and femoral vein being anastomosed in such a manner that the vein will receive the arterial blood. Wieting and others have reported successful results, cures of impending gangrene and restoration of circulation. Experimental work, however, (Stetten) would tend to show that it is practically impossible to transform the veins into arteries by anastomosis, and clinical reports do not justify us in recommending this method either in the presence of gangrene, or in threatened gangrene. Involvement of the veins in thrombo-angiitis obliterans, both superficial and deep, with obliteration in a larger percentage of the cases, makes it unlikely that improvement of circulation could occur by deflecting the arterial current into the veins.

¹ It is interesting to note that an apparatus for mechanically producing intermittent Bier's venous hyperemia was used in Germany during the Great War, in order to combat infection in limbs infected with the gas bacillus. The compressing cuff is distended by pressure from an oxygen tank, and a mechanical timing interrupter breaks and makes the flow of gas, causing the dilatation of the cuff. It is possible to employ a similar apparatus for the intermittent and isolated compression of single large arteries. A small electric motor may furnish the power for air pressure, and a pneumatic cushion may be so adjusted as to compress the femoral artery.

Not only theoretic consideration but also practical experience have been convincing in demonstrating the futility of attempting arteriovenous anastomosis in this disease. Thus we may cite the following instructive instance of:

Functional failure of arteriovenous anastomosis; bone formation in, and occlusion of anastomosed area.

Case L. W., age 32, Russian Hebrew, June 15, 1913, says that he has been troubled for two years with pain in the right leg. He had had an arteriovenous anastomosis done at the Beth Israel Hospital on November 5, 1912, but he did not feel improved by the operation. On physical examination, June 20, 1913, the right foot was considerably enlarged by reason of edema, cyanotic, very painful, showed some atrophy, marked ischemia in the elevated position.

On June 23 the patient begged for amputation because of the pain. The author decided to expose the site of the anastomosis both for purposes of discovering what had occurred and possibly whether another anastomosis was feasible. A considerable amount of scar tissue was found about the situation of the vessels. The artery and vein were embedded in a mass of connective tissue. They were liberated with some difficulty and a piece of artery and vein, three inches in length, was excised. Both the artery and vein for a distance of five inches were found converted into hard pipe stem-like cords.

Histological examination showed complete obliteration of the vessel by connective tissue and bone formation.

When this condition was found at operation, it was decided to proceed with amputation. A Gritti-Stokes was done with an excellent result.

In view of the bad outlook in these cases, it is not to be wondered at, that even peri-arterial sympathectomy of the larger arteries (femoral) should have been suggested and tried. The author has elsewhere called attention to the fact that little can be expected from such an operation on *a priori* grounds.

Strauss¹ reports decortication of the right femoral artery for a distance of 8 cm. in a case of thrombo-angiitis obliterans. Although the pain is said to have been influenced for a short time, gangrene soon supervened and pain returned. From the experience in this and another case, this author concludes that the consequent vasodilatation is only transitory, and that the beneficial results are only temporary.

Limited Amputation.—Amputation of a toe alone is often unsuccessful for healing may not take place. In some instances, however, conservative treatment such as described above, together with ablation of a toe alone, or several toes if necessary, may be followed by good results. In the majority of cases amputation at a point higher up will be necessary.

Radical Amputation.—In the majority of cases amputation of at least a portion of the leg will become necessary. The Gritti-Stokes amputation is the ideal procedure in these cases, although lower amputations are occasionally successful. The author found that in a series of 65 amputations according to the Gritti-Stokes method primary union was obtained in all instances.² When amputation is performed lower down, healing may take place, but in many instances sloughing of the flaps occurs, and secondary amputation becomes necessary. Inasmuch as the disease occurs for the most part in poor working people, it seems that the Gritti-Stokes amputation is preferable to those methods which are dubious in their outcome and require many months for the accomplishment of their purpose. Methods or tests for estimating the point at which amputation should be done are all unreliable.

Some surgeons would prefer circular amputation through the lower part of the thigh, if, in their experience a better artificial knee joint can be thus applied. The author has had eminently satisfactory results with the Gritti-

¹ Strauss, Surg., Gynec. & Obst., Feb., 1923, 36, p. 290.

² In one case the patient died of pulmonary embolism about eight days after the operation.

Stokes amputation. Whenever complicating ascending lymphangitis or severe infection is present, the amputation must be done much higher through the thigh.

THE SELECTION OF THERAPEUTIC PROCEDURES

Here, as in the arteriosclerotic cases, careful attention to details and proper clinical inferential reasoning will help us select a combination of methods that may ward off gangrene or even give considerable comfort to the patient.

The cases with minimal symptoms, coldness of the toes or foot, possibly intermittent claudication, with or without spontaneous pain, are those that should receive special consideration. For, with intensive prophylaxis, correct appreciation of the gravity of a seemingly minor affection, the patient's limbs may be preserved for many years and their utility prolonged or made permanent. It is advisable to recommend, in such cases, a preliminary "cure" or treatment in which absolute rest in bed is required for at least 4 to 6 weeks. During no part of this time is the patient allowed to walk, although after the first 2 weeks it is well to permit the shoes to be put on for $\frac{1}{2}$ hour a day, provided the latter do not constrict or hurt in any way. Smoking is prohibited. Injections of sodium iodide are given intravenously, and if we wish, flushing of the alimentary canal with Ringer's or Locke's solution through a duodenal tube may be given a trial. This method has been recommended (W. Meyer) to decrease the viscosity of the blood.

The greater part of the day is occupied with the manipulations for enhancing the circulation, namely, the postural and hot air methods. The former should occupy every other hour of a 16 hour day, excluding an hour's rest for lunch and dinner and should alternate with similar periods of hot air treatment (about 40 minutes each). Restriction of one or the other may be found necessary by virtue of special reactions of the patient.

After the 4 to 6 weeks, the postural and hot air séances are to be continued for about 6 hours a day (each 3 hours), the distribution of application being adjusted so as to suit the patient's habits. As improvement occurs, reduction in the daily duration of treatments is in order, a more intensive resumption of the same being indicated upon the slightest recurrence of symptoms.

When the patient is willing and able to coöperate, intermittent compression of the femoral artery for 30 seconds every 5 minutes over hourly periods, may effect the same reaction as the postural treatment, and enhance the circulation.

When *migrating phlebitis* is present, we must distinguish between the mild and the severe cases. Whilst in the former, the postural and hot air treatments may find no absolute contraindication if carefully carried out and in reduced measure, absolute rest alone with wet dressings and warmth are the best means of alleviating the symptoms in the more severe cases.

In the more advanced cases with trophic lesions, we must treat the circulation and the local sequelæ of disturbed nutrition. Where pain is not intensified by the changes of position of the limb, the postural method may be carried out as above described. But careful attention must be given to the rapidity with which blanching sets in on elevation, lest we unduly prolong the time of anemia. So, too, the reactionary rubor may be attended with pain, whose advent may require abridgement of the period of pendency.

Where dry gangrene is present, we combine the postural, hot air, prophylactic measures and intravenous medication. But when ulcers, infection, or

retention of secretions under a nail are observed, the continuous or multiple baths of hypertonic salt solution may be invaluable. We should not fail to cut away a dead nail that favors retention of secretions in spite of the patient's remonstrance. We must then try out whether permanent baths or intermittent baths alternating with 40-60 minutes of postural exercises are the best combination in any given case.¹

Where there are trophic lesions, the intermittent warm baths are so valuable as to warrant a trial in every case. The water is kept at 90° to 98° F., the temperature being varied according to the patient's ability to endure local moist heat. The methods of employing baths that are advocated by the author are the following: The limb is immersed therein during the dependent phase of the cycles of postural treatment for half hour or hourly periods. Immersions are arranged so as to alternate with the postural exercises and banking.

When conservative methods fail, or there is a fulminating type of gangrene, when severe infection complicates, or from the very outset larger areas become mortified, amputation will be indicated.

CHAPTER LXVI

ATHERO- OR ARTERIOSCLEROTIC DISEASE—CLINICAL MANIFESTATIONS

The clinical picture resulting from intense arteriosclerotic disease of the vessels of the extremities, particularly of the lower extremities, is attributable to the effects of impaired or even arrested circulation in arteries whose lumina have become narrowed or completely obstructed. By virtue of proliferative changes that occur in the walls of the vessels, particularly in the intima, and because of the deposition of atheromatous and calcareous material, the arterial lumen becomes gradually narrowed, and the normal elasticity of the vessel walls becomes lost. In addition to the two factors, obstruction by hyperplastic products and loss of normal elasticity, *occlusive thrombosis* may be superadded, these three elements being responsible for the circulatory changes in the diseased arteries.

Although gangrene is the most striking and most severe termination or outcome, when the vessels of the lower extremities are afflicted with intense and extensive arteriosclerosis, the evolution of this final stage is for the most part gradual, the affected limb passing through a number of *prodromal stages*, in which definite evidences of defective circulation can be detected. *These clinical stages should be recognized and properly appreciated, for, then only can the proper prophylactic measures be instituted to delay or even prevent the development of the mortifying process.* The most important of these clinical pictures are briefly the following:

Clinical Forms of Arteriosclerotic Disease of the Lower Extremities.

1. *Intermittent Claudication.*—This symptom may be the only indication of arterial disease. Intermittent claudication may be the only manifestation of obstructive disease of the arteries, or, it may be associated with absence or

¹ For further details, see Chap. LXXIII, Treatment of Arteriosclerotic Disease of the Vessels.

pulsation in the dorsalis pedis, or posterior tibial, and popliteal arteries. Later on, it is overshadowed by other symptoms. *It is not to be regarded as a disease per se, but as one of the manifestations of a number of diseases in which the arteries of the lower extremities are narrowed or obliterated.*

2. *Intermittent Claudication with Other Evidences of Arrested or Impaired Arterial Circulation.*—Such other phenomena are ischemia on elevation, possibly also erythromelia or reactionary erythromelia, attended in some instances with coldness and paresthesiæ. Vasomotor symptoms are not uncommon.

3. *Cases without Trophic Disorders.*—Pallor of the foot in the horizontal position, or increased pallor on elevation, and moderate or fairly marked hyperemia, rubor or erythromelia in the dependent position with absence of pulses, may be associated with coldness or occasional cyanosis, in patients who may or may not have had symptoms of intermittent claudication.

4. *Cases with Trophic Disorders.*—In cases with *intermittent claudication*, ischemia on elevation, rubor, coldness, paresthesiæ, *absent* pulses in certain vessels, *trophic disturbances* in the form of ulcers may develop, slowly or suddenly after exposure to cold or some other insult.

5. *Chronic Cases with Inability to Walk.*—These may have been preceded by intermittent claudication. There gradually develops chronic rubor, inability to walk, and pain in the foot. The usual signs of impaired circulation can be elicited. In short, the picture is that of a chronic erythromelia, sometimes with edema, without trophic disturbances, but with moderate or even intense pain.

6. *Cases with Attacks of Thrombosis.*—With any of the above pictures or preceded merely by indefinite history of intermittent claudication, sudden thrombosis may occur in some of the larger vessels, giving rise to the following symptom-complex. The patient will be attacked by sudden pain in the calf or in the foot, with inability to walk, and with pallor and coldness of the forepart of the foot. On examination, the blanching is seen to be intense upon elevation, the dorsalis pedis and posterior tibial arteries may be pulseless, whilst the vessels of the other leg are pulsating. After a variable period of time, gangrene may set in, or indolent trophic disorders may develop. In other cases a condition of *chronic rubor* may result, with gradual return of circulation, the usual physical signs of impoverished circulation persisting. Careful treatment instituted at the very inception of the thrombotic attack, may ward off threatening gangrene.

In short, the prodromal signs of gangrene, namely, symptoms that may precede by days, months or years, the development of the mortifying process, are in the main: intermittent claudication, paraesthesiæ, pallor, coldness, pain, chronic rubor (erythromelia) in the horizontal and dependent positions, attacks of thrombosis, blanching in the elevated position of the limb or even in the horizontal position, loss of pulsation in the dorsalis pedis and posterior tibial, sometimes in the popliteal, more rarely in the femoral arteries, and trophic disturbances such as ulcers, fissures, impaired nail growth, atrophic skin and edema.

Amongst the more unusual types of clinical course the following (7 and 8) warrant recording.

7. *Cases with Obliteration of All the Pedal Arteries, Popliteals and Femorals.* After a longer or shorter period of intermittent claudication lasting months, sometimes years, severe almost continuous pain may be localized in one or both feet, with occasional radiation in the leg or lower thigh. The objective manifestations in one case were the following.

The left foot was in a condition of very slight erythromelia, some puffiness of the dorsum of the foot and the toes. The leg was markedly atrophic, particularly the muscles of the calf, the skin being fairly well preserved. The whole foot seemed to be tender to the touch. There was no marked coldness of the foot, except the big toe, the temperature of which was manifestly reduced.

In the dependent position there was fairly marked rubor of the left foot, none of the right, although pulsations were absent on the right as well as on the left. On elevation there was distinct ischemia of both feet to a slight degree.

The striking features of this condition are the inability to walk, continuous pain in the foot, with atrophy of the corresponding calf, and the absence of all the pulsations in the lower extremities. The difference in the subjective



FIG. 127.—Arteriosclerotic gangrene.

and objective manifestations in the two legs of the above case can only be accounted for by differences in the development of the collateral paths.

8. *Chronic Gangrene with Atrophy*.—Extensive obliteration of the arteries of the lower extremities may lead to a picture of chronic atrophy associated with slow development of gangrene that may persist for months or years without infection and without complicating moist gangrene. It is interesting to contrast the persistence of large gangrenous areas in these cases, with no tendency to inflammatory process in the neighborhood, with the rapid develop-

ment of fulminating putrid gangrene in many of the embolic and thrombotic cases following infectious diseases and pneumonia. In the latter, possibly by virtue of the liberation of ferment, be it through the presence of bacteria or their toxins, secondary bland thrombosis develops rapidly in the deep veins. In the cases under consideration, however, such venous occlusion is absent, and a withered condition without infection ensues.



FIG. 128.—Arteriosclerotic gangrene.

It is noteworthy that a senile condition is not necessarily present, and the atrophic state may appear in patients in their early fifties or even in the late forties.

An exquisite example of such a process was the following:

L. S., 54 years of age, does not remember having had any trouble with his limbs until the right leg was injured by a fall from a horse (chronic arterial disease, doubtless with

obliteration without symptoms). A wound over the right shin resulted, which necessitated a small operation, the nature of which he does not remember. Since then the wound has not healed. He has not been able to use the right leg, has been bedridden, and the condition of which he now complains has developed.

The area operated upon showed no tendency to heal, and a slow gangrenous process developed that spread over the greater part of the shin bone, the latter protruding through the skin. Until recently almost two-thirds of the length of the bone could be seen through the self-enlarging wound. For several months he has also had trouble with the left leg, a change in the appearance of the toes having been noted, and the foot being cold.

Physical Examination, March 1, 1921.—Both feet and legs are markedly atrophic (Figs. 127 and 128). The anterior aspect of the right leg over the middle two-thirds shows extensive dry gangrene of the skin, the antero-lateral and antero-internal surfaces of the tibia presenting through a large aperture or defect, being dry, gangrenous, like dry bone outside of the body cavity. All the toe nails show hyperkeratosis, discoloration, and there is marked atrophy of the skin. At the knee there is an area over the outer condyle of the femur, over which the skin has become mummified (dissecting room type). There is cyanotic and reddish discoloration of the left foot, and the skin of the whole leg is so withered that there seems to be little or no circulation in it, but gangrene is threatening.

March 14, 1921, amputation of the right leg through the upper third of the right thigh. This was followed by sloughing of the flaps.

During his stay at the hospital the left foot became spontaneously gangrenous, mummification ensuing.

April 11, 1921, the patient left the hospital against advice.

Special Symptoms. *Erythromelia of Upper Extremities in Arteriosclerosis.*—Just as intermittent claudication may involve the upper extremities (dysbasia angiosclerotica) so also is a condition of rubor occasionally observed. Of the author's atherosclerotic cases with marked rubor of the hands or hands and feet, the preponderating number seems to have occurred in diabetics. When such erythromelia is a striking phenomenon, then ischemia on elevation can also be elicited. As a rule, blanching of the hands is relatively more difficult to produce by postural changes than its analogous condition in the feet and legs, so that an extensive infringement upon the patency of the vascular channels can be prognosticated, whenever rubor and pallor are exaggerated in intensity.

A narration of a typical case may not be amiss here, because of the general trend amongst internists to attribute marked rubor of the hands only to erythromelalgia and other vasomotor neuroses, and because such rubor as an expression of compensatory efforts attending organic vascular lesions, is so often ignored.

Atherosclerosis, diabetes, chronic erythromelia of hands and feet.

Case R. B., Austrian, male, aged 57 years, says he has had diabetes for six years. For the last six months the left hand has been swollen. Both hands get red and painful in the pendent position. He observed this symptom first in the feet. Six months ago he had redness of the tips and borders of the hands; three weeks ago the redness passed above the wrist. Warmth seems to increase the pain whilst cold air makes the hands feel better. There have been no ulcers of the fingers. Eight days ago he had a mild apoplectiform attack during which he could not speak for one-quarter of an hour.

He complains of sticking pains in the borders of the hands and in the fingers with neuralgic pains radiating upward. On some days the hands look almost normal and then there is no pain. There are exacerbations which last days.

Physical Examination: Hands.—Both become pale when elevated to 135° , and become markedly scarlet when hanging down. The redness extends up three inches above the wrist on being pendent for a few minutes. There is slight cyanotic discoloration. The inner borders are most intensely red. The hands look swollen and puffy, especially over the palmar aspect of the left. Both hands feel fairly warm. There are areas of cyanosis over the palm, especially over the tips of the fingers. Squeezing the fingers hurts more than normally. His hands do not feel better when raised, the pulsations being about the same as when in the horizontal or pendent position. *Both radial pulsations are absent.*

The brachials and axillaries: Right feels *calcareous* and pulsation is only felt in the upper third. Left also *calcareous* and pulsation felt in the upper two-thirds.

Lower extremities: Have the typical appearance of the atrophic condition usual with atherosclerotic vessels. Slight erythromelia of the feet in the pendent position; no trophic disturbances.

Femorals: Both exhibit fair pulsation but are very hard.

Popliteals: Right faint; left absent.

Posterior tibial and dorsalis pulses not palpable on both sides.

In the elevated position, even after ten minutes, there is only very slight ischemia. Right leg is slightly paler than left. There is only a very slight induced erythromelia, more on the left than on the right.

Erythromelia of Lower Extremities.—The clinical picture of a red painful leg, so characteristic of long standing impairment of the circulation attending marked atherosclerosis with or without diabetes, is worth mentioning and illustrating by a clinical case, for differentiation from thrombo-angiitis obliterans and erythromelalgia (Weir-Mitchell) will thereby be clarified.

Usually, the *clinical symptom-complex* comprises a history of long standing intermittent claudication, with or without previous trophic disorders, possibly an attack of arterial thrombosis without gangrene as a sequela, and finally a condition of *painful red leg*, with atrophy. Edema due to renal disturbances or cardiac insufficiency may complicate:

Erythromelia (red leg) in an arteriosclerotic.

L. S., male, 83 years of age, has had cramps in his left leg for many years, and 1 year ago an attack of severe pain in the left foot. He has been troubled for about 6 months with a condition which gives him concern both because of the evident discoloration of the leg, and because of the attendant frequent pain and discomfort. His wife says that the pain, the redness and the coldness of the leg to the touch are the chief noticeable changes.

Physical Examination.—The whole of the left foot and part of the leg is markedly red, both in the horizontal and pendent positions, the region of the fifth toe being tender. Elevation of the limb intensifies the pain in the foot. There is slight edema. The popliteal, posterior tibial and dorsalis pedis pulses are absent. There is no gangrene.

Vasomotor Phenomena.—The nervous mechanism with which arteries are endowed and which modifies their reactions to blood pressure, is a potent influence wherever local circulatory impairment has taken place. We have already alluded to the peculiar vasomotor lability and instability attending obstructive arterial lesions. Allbutt¹ is not in accord with the oft repeated impression that the superficial vessels in arteriosclerotic cases are even more liable to spasm than the healthy. According to this author, plethysmographic experiments upon the arm in arteriosclerosis, and observations carried out by more than one skilful investigator,^{2,3} indicate that the response of the vasomotor mechanism to stimulation is not enhanced but diminished.

Whatever the value of artificial methods for gauging the vasomotor excitability, the author is convinced from clinical experience that an increased susceptibility or tendency to *vasomotor phenomena* on the part of the smallest arteries is often present in the cases in which obstructive arteriosclerotic disease of the extremities is present. He is in accord with the view that the larger arteries do not participate appreciably in effecting the manifestations, agreeing, therefore, with Albutt in this regard. But in the more peripheral arteriole and capillary territory, a distinct accentuation of vasomotor fluctuation occurs that suffices to give noticeable symptoms.

Trophic Disturbances and Gangrene.—It is important to distinguish between the two large groups of tissue disintegration, which result from imperfect and arrested circulation, first *trophic disturbances*, and second, *gangrene*.

¹ Allbutt, *Diseases of the Arteries* (Macmillan, 1915).

² von Romberg, *Deutsch. med. Wchnschr.*, Oct. 28, 1909.

³ Müller, O., *Deutsch. med. Wchnschr.*, 1906, 38-39.

1. *Trophic Disturbances*.—Trophic disturbances include all manifestations of impaired nutrition of the skin and its adnexa, and may develop months or years before gangrene is established. They occur much less frequently in arteriosclerosis than in thrombo-angiitis obliterans.

The skin may be atrophic or withered, and the nails may show evidence of impaired growth. Ulcers at the tips of, or between the toes, the sequelae of abrasions or small wounds, are occasionally found. More rarely, punched out indolent ulcers over the dorsum of the foot, or over the lower half of the leg, may be complications of attacks of extensive thrombosis.

Small bullae, the precursors or prodromal signs of small patches of gangrene, may lead to ulcers or to the separation of a nail. They may heal, or may lead to extensive gangrene. Perforating ulcers more often attend the diabetic cases of arteriosclerosis, and are to be found most frequently over the plantar aspect of the foot. They are chronic in their course, and often associated with deep necrosis and suppuration. When they involve the toes, they lead to necrosis of bone. The toe may become enormously enlarged. A granulating strawberry-like wound may be formed, which lies at the orifice of a tract leading down to dead bone.

A bunion at the metatarsophalangeal joint of the great and fifth toes, not infrequently affords a good nidus for an ulcer which almost always leads to necrosis of the underlying bones.

Small ulcers, of the perforating variety, near the base of a toe, often represent the orifice of penetrating abscesses, the necrotic and suppurative process extending along the tendons and bone, and causing necrosis of bone for a considerable distance beyond the site of the wound.

In the case of the *upper extremities*, trophic disorders associated with arteriosclerosis are very rare, and their presence should, therefore, suggest either the existence of thrombo-angiitis obliterans, vasomotor disease, or other neuropathic cause. Gangrene, too, of the upper extremities is exceedingly rare, though a symptom-complex comparable to intermittent claudication in the lower extremities is occasionally encountered. In rare cases there may be intense rubor of the hand. The radial artery may fail to pulsate and can be palpated as a rigid cord. X-ray examination will reveal intensely calcified arteries, or at least calcareous deposits along the course of the larger vessels.

2. *Gangrene*.—Although it is most commonly seen in the aged and, therefore, has been termed *senile gangrene* (chronic or Pott's gangrene), it may also afflict younger individuals between the ages of 40 or 50, when the atherosclerosis is precocious in development, or when a secondary thrombosis occurs early in the disease. In most instances dry gangrene develops. In some, however, we may see the moist type or combinations of the two.

Dry gangrene usually involves the toes, the big toe being the site of predilection. Or, there may be multiple areas of gangrene involving the peripheral parts, and in the more severe cases, extensive dry gangrene of the greater portion of the foot may be expected. The process may be a slow one, the toes being spontaneously amputated or removed by operation. The extent of the gangrene cannot be exactly estimated in the atherosclerotic and diabetic cases, from the external appearances, nor from the line of demarcation when it is present. For, if such an amputated limb be dissected, extensive, widespread sloughing of the deeper tissues with necrosis of bone extending for a considerable distance beyond or above the apparent line of limitation, will often be revealed. It is incumbent upon us, therefore, in every case to make an X-ray examination of the foot, as this may demon-

strate that the destruction has implicated tissues beyond the zone of skin involvement.

Where infection is superadded, the usual signs of phlegmon formation or lymphangitis will be in evidence. The suppurative inflammation will spread into the healthy tissues from the site of the gangrene, either in acute fashion, or subacutely without causing any considerable rise of temperature, but evoking intense pain.

Moist Gangrene.—Early evidences of threatening gangrene will be intense cyanosis, coldness of the affected part, usually the toe, and the appearance of a hemorrhagic bleb or a number of blebs filled with pinkish serum. The part will have a dark bluish or purplish appearance, or even angry red where the epidermis becomes lifted off. In the immediate neighborhood, there will be ecchymoses over smaller or larger areas, and edema with exquisite tenderness just above the mortifying tissues. Where there is infection, the typical signs of lymphangitis usually following the course of the internal saphenous veins will be encountered. In later stages the epidermis becomes detached, is folded, and hangs loosely in places.

In some cases there will develop spontaneously a number of large bullae over the toes or dorsum of the foot, and, in these, clear or bloody serum alone will collect. This is the early stage of moist gangrene. As the gangrenous process extends, all those changes that have been previously cited and described under moist gangrene will make their appearance. If infection occurs, the phlegmonous process is more rapid and intense than in the case of dry gangrene, and particularly in diabetic cases will the resistance on the part of the body be inadequate, and the inflammatory process difficult to check.

Clinical Course in Athero- or Arteriosclerotic Disease.—Although the variations from the given types are manifold, and it is, therefore, impossible to recount all the various types of clinical course, the following summaries include the most common. Many patients have intermittent claudication and pain on walking for a long time, then develop coldness of the toes or of the whole foot, paresthesiæ, but rather rarely are afflicted with ulcers or other signs of trophic disturbance so characteristic for the disease, thrombo-angiitis obliterans. They may have attacks of thrombosis, complicated with ulcers or patches of gangrene, or such attacks may be followed by healing and *a state of chronic erythromelia* with discomfort and some disability in the affected leg; or, practically all symptoms may be absent until after some insult, traumatism or cold, or without cause a patch of dry or moist gangrene develops. In a number of cases, particularly in the diabetic, a perforating ulcer brings the patient to our notice, and this is complicated by necrosis of bone and the usual signs of deep infection. Many patients complain only of disability, particularly difficulty in walking. Some develop an ulcer of the nail-bed with a patch of dry gangrene that heals.

Others never develop gangrene, but the signs of insufficiency of circulation are manifest if the limbs be examined as, blanching on elevation, slight erythromelia, and absence of pulsation are regularly present.

The author has made an observation that these latter patients are prone to fugitive attacks of erysipeloid infection of the feet and legs, or mild lymphangitis with short periods of fever. Perhaps diminished resistance of the inadequately nourished territories predisposes to such complications.

When gangrene develops—usually of the dry variety—the onset is often ascribed to some previous injury, the paring of a corn, the wearing of too tight a shoe, exposure to cold, a bruise or the application of some strong medicament. The big toe is usually the first to be involved. Its tip or the whole of it

becomes dusky red or purple, gradually becoming purplish-black. These changes in color and evidences of mortification are attended with intense pain in the affected region and in the foot. If the gangrene remains dry and no infection takes place, mummification ensues, the toe becoming dry and shriveled, into a hard black mass. This, however, may be associated, as referred to above, with necrosis and suppuration in the depth. A line of demarcation may form, or gangrene may spread, depending upon the presence or absence of infection, the resistance of the tissues, and the condition of the arteries.

Clinical Forms of Trophic Disorders and Gangrene.—So variegated are the clinical pictures presented by the various types of nutritive disorders complicating arteriosclerotic closures of the vessels of the extremities with or without thrombosis, that but a very few types can be mentioned here.

The following review will aid the clinical recognition of this condition.

1. After the removal of a corn by the chiropodist or by the patient himself, or after the slightest cutting injury a small focus of pus develops, the toe becomes red and cyanotic either through inflammation or stasis, and gangrene of this part soon ensues.

2. A blister or larger bulla that is more than usually painful develops over a toe, or on the dorsum of the foot, the epidermis is cast off leaving a discolored derma which becomes bluish black, and then gangrenous.

3. Or, the bed of the nail begins to bleed, possibly attended with the formation of a blister or bleb at the distal margin of the nail, or with more or less chronic suppuration. And finally, when the nail becomes completely separated, the gangrenous area or extensive slough is seen to lead down to bone.

4. After a longer or shorter period of prodromal symptoms, particularly intermittent claudication, chronic blueness or cyanosis affects some of the parts, particularly the big toe. Days or weeks pass, then ulceration and gangrene terminate the picture.

5. Although the big toe seems to be the site of predilection in arteriosclerotic cases, gangrenous patches may develop anywhere: over the dorsum of the foot, over the heel, often in the neighborhood of calluses or fissures. When these become infected, attacks of lymphangitis or deeper infections are not infrequent complications.

6. Atypical forms of ulceration of the indolent type are not uncommon. Multiple ulcers were observed in a case that gave a typical history of intermittent claudication and pain in the feet, there being marked ischemia and intense erythromelia. There were shallow, punched out, indolent ulcers over the dorsum of the foot, most of them no larger in diameter than a quarter of an inch, the result of the separation of the gangrenous patches of skin, their margins showing no tendency to heal, and no reactive hyperemia. Such ulcers may persist for a long time until finally, by reason of a fresh accession of thrombosis in the deep vessels, or some mechanical or thermal cause, extensive gangrene of the foot occurs necessitating amputation.

7. Occasionally there is a history of the existence of previous ulcers that have healed, with a complete repetition of the clinical course.

8. The big toe may be found in a condition of chronic granulation and ulceration, being enormously enlarged, almost twice the size of normal, presenting a large granulating strawberry-like surface at the center of which a sinus may lead to dead bone.

9. A type is also encountered in which trophic disorders in the form of ulcers are present, is followed later by dry gangrene involving all the toes.

Hemorrhagic or purple spots appear, are painful, and then may become the seat of gangrene.

10. The whole foot may be in the state of very intense erythromelia, it being almost a vermilion red, except over the area of trophic disturbances or gangrene when such are present. Many of the various forms of trophic disorders may be associated with this intense rubor.

11. Cases with patches of dry gangrene give a history of discoloration and pain over periods of weeks or more. A small purplish or cyanotic spot develops, particularly over a toe, and then this process after the elapse of many days, may extend rapidly over to the rest of the toes and foot and eventuate in a condition of dry gangrene.

12. A type with extensive dry gangrene, shows mummification of all of the toes, and portion of the dorsum, as well as the sole of the foot. The rest of the foot, when not involved, is very cold, presenting a cyanotic and hemorrhagic discoloration. In other cases where the line of demarcation is distinct, there is no evidences of progressive gangrene above the line. In addition to the large area of gangrene, corresponding areas of poor circulation are found. In other cases there is complete ischemia for a distance above the demarcation, or hyperemia depending upon the condition of the circulation.

13. Cases with the development of *moist gangrene* usually develop large blebs over the dorsum of the foot and toes, the various toes showing different types of lesions. There may be extensive cyanosis of the toes, coldness, with blackish discoloration. The epidermis becomes lifted off by a collection of serum and blood, and certain toes show only cyanosis or black blebs, all of these being in various stages of the gangrenous process. If inflammation is present, intense hyperemia of the dorsum must be distinguished from the erythromelia. The dorsum of the foot also may show discrete patches of gangrene, cyanosis and hemorrhagic blebs. Phlebitis and lymphangitis may accompany this picture, so that when a cross section is made along the course of the internal saphenous vein after amputation, pus can be expressed out of the lymphatics.

14. Cases with chronic gangrene and atrophy. Where the limb or limbs become wasted and almost shrivelled up, a chronic form of gangrene lasting for a year or more may give a remarkable picture. In such cases the greater part of the tibia may present in dried form through a large wound that is the result partly of trauma or the result of whatever cause. The foot or feet may be almost intact, with, or without gangrene of the toes, but atrophic, cyanotic or red, with the patient bedridden for months and years.

CHAPTER LXVII

ARTERIOSCLEROSIS—PATHOLOGY

Pathogenesis.—Arteriosclerosis according to Marchand¹ is a deteriorative disease of the vessels. Because of the exquisite fatty changes that occur in the vascular walls, the affection was termed “atherosclerosis” in contradistinction to the old name “arteriosclerosis.” The latter term was first employed by Lobstein in view of the hardening of the vessel wall. The

¹ Marchand, Verhandl. d. 21 Kong. f. inn. Med.

appellation "endarteritis" was coined by Virchow as descriptive of a reactive hyperplastic lesion of the intima.

The more recent observations of several authors (Jores, Marchand and others) interpret arteriosclerosis or atherosclerosis in the light of effects of deterioration resulting from stresses and wear. Marchand views atherosclerosis as a progressive nutritional disturbance of the vessel wall, accompanied by thickening and sclerosis of the intima, multiplication and degeneration of the cellular elements, partial necrosis, and finally disintegration and calcareous degeneration. In the arteries of the extremities the media is particularly implicated in the degenerative process.

Recent authorities lean to the view that the peculiar alterations are the results of nutritive derangement, that is evoked by the excessive functional stresses. In this sense one would interpret atherosclerosis rather as a deteriorative disease due to wear and excessive use, rather than as purely a senile change. The deleterious factors (mechanical factors) do not usually attain sufficient intensity until a certain age is reached; for, cumulative action through many years is required to bring about the necessary arterial responses. From the varied distribution of the process in the vascular system, it would appear that the individual suffers in those vascular territories which are most subject to strain in the respective case.

In the light of most recent investigations, the proliferative and degenerative processes in the intima and media are expressions of the same disease, and the very histologic forms depend upon the particular structure and function of the vessels involved.

In the evaluation of such a deteriorative disease, we must not forget that the end products, we are wont to see, are elaborated over many years. To investigators, such as Aschoff,¹ must be given considerable credit, for their demonstration of the manner in which the characteristic changes are produced from the normal embryonal arterial types up to the markedly degenerative senile products. The arteries are in no essential sense different from other organs in which the process of building up attains a certain climax, and in which the process becomes stationary for a certain period, only to undergo regressive subsequent deterioration. Furthermore, it is known that the structural development of the various organs attains its height at varying periods and this seems to be true also in the arterial system. Aschoff through his embryological studies demonstrated clearly that a comparison of the embryonal arteries with the pictures they offer during early infancy, afford enough similarity to warrant the assumption that the later changes are but intensifications of these with secondary regressive degenerative lesions.

It would seem well, therefore, for a clear understanding to approach the subject with a description of the arteries of the embryo, those of the child, and those of the adult. For this the reader is referred to the chapter on Histopathology of Arteriosclerosis.

We need not discuss here the many theories as to the pathogenesis of athero- or arteriosclerosis. Histologic studies have demonstrated that the beginnings of arteriosclerosis are recognizable even during youth. These, however, do not necessarily develop into a diseased process. The alterations that correspond to the aging process do not constitute a disease *per se*, but a manifestation of deterioration. Although all individuals show the well known evidences of arterial deterioration, only some develop a progressive

¹ Aschoff, Ueber Entwick. Wachs. u. Alt. Vorgänge a. d. Gefässen, (Fischer—Jena, 1909).

process of sufficient intensity to be regarded as true arteriosclerotic or atherosclerotic disease.

Potent as the mechanical stresses may be in the production of the degenerative and hyperplastic changes in the arteries, these moments, as well as those of deterioration, cannot altogether explain all of the histologic changes observed. If we extend the term *deterioration* to include all of the influences that arteries are exposed to during life, we have a term so comprehensive that it would naturally include forces of diverse variety. As such, deterioration would include a complex of influences, in which not only physical, but also chemical factors, would be engaged. In addition to the generalized wear and tear that all tissues undergo, the arteries must be affected (Hueck) by additional factors in order that the lesions known as athero- and arteriosclerosis be elaborated. Nor can we accept the view that the causal moments must necessarily be uniform in all cases. Perhaps the special changes, such as calcification, depend upon additional toxic factors. Therefore, in this complicated problem it is impossible to estimate to what extent each of the many causal moments participates in the production of the end result.

The researches of Jores¹ because so important, deserve more than mere passing mention. According to this author, the changes in the intima although not the only lesions of arteriosclerosis, are the essential alterations; and an explanation of the intimal thickening will also throw light on the pathogenesis of the whole process.

Heubner from a comparative study of syphilitic endarteritis of the brain arteries and arteriosclerotic vessels, had concluded that the latter process suggests true hypertrophy of the intima with proliferation of existing elements, especially the elastic lamella, so that the architecture of the intima of small arteries approaches that of the normal larger ones. All the secondary processes, such as fatty degeneration, calcification, are to be considered essentially regressive in character, and as unimportant in so far as pathogenesis is concerned.

Jores has laid special emphasis on two types of elastic lamellae in the intima. The first variety shows reduplication of elastic fibers in a manner that suggests a cleavage of the membrana interna elastica, with splitting off of fibers, and is characteristic of the arteriosclerotic process. In the second type, new formed fibers of more delicate composition appear.

The author in his first publications on the histopathology of thromboangiitis obliterans² had noted and emphasized the difference between the new formed elastic fibers in the obliterating tissue of thromboangiitis obliterans, and those so peculiar to the hyperplastic lesion of arteriosclerosis. So also, Jores had observed a similar discrepancy in the thrombosed arteria fossae Sylvii of a case, and in the experimentally produced endarterial lesion following ligation. The aforementioned peculiarities are specific in his opinion. The hyperplastic intima associated with certain thromboses and ligation, shows also a multiplication of elastic elements. But this corresponds to the proliferation seen under other circumstances and in other tissues. The process characteristic of arteriosclerosis is initiated by thickening of the internal elastic lamina and consequent cleavage, a lesion that has no analogy elsewhere in the body.

Elastic Fibers in the Normal Arteries.—For a correct comprehension of the pathology of elastic fibers of the arterial intima, a knowledge of the normal is a sine qua non, especially since variations in the thickness of this

¹ Jores, L., Wesen u. Entwicklung d. Arteriosklerose, Wiesbaden (J. F. Bergmann), 1903.

² Buerger, Pro. N. Y. Path. Soc., Feb. & Mar., 1908.

coat, its elastic fiber content and even reduplication of these lamellae may occur.

In the newborn and in young infants, the intima is made up merely of the internal elastic membrane, and the endothelium. A musculo-elastic layer is only found at the bifurcations of the small arteries. Where vessels are given off, small protuberances made up of such tissue project into the vessel lumen. A longitudinally disposed muscle layer is inserted, as it were, at certain places between two laminae of the internal elastic membrane. Of the two elastic layers, the inner is more prominent than the outer, and conserves the general course of the vascular fibers. Within these elastic lamellae are enclosed not only the longitudinal muscle bundles above noted, but also finer elastic fibers. This complex structure in its entirety simulates, as can be readily seen, the lesion of intimal thickening characteristic of the arteriosclerotic process.

Although first limited to the wall near the angles of vascular offshoots, the duplication of elastic fibers soon extends longitudinally, so that cross sections will find it at situations independent and far removed from points of bifurcation. Spreading even in a circular direction, pictures are produced in which a greater part of the circumference of the vessel wall is occupied by this process.

Such normal variations of the internal elastic membrane do not appear to vary in intensity according to age.

In short, a thickening of the intima indistinguishable from that occurring under certain pathological conditions, is elaborated in the normal, probably as a reactive response to functional demands.

Both in physiological and pathological hypertrophy of the intima, there is a concomitant appearance of nuclei between the layers undergoing cleavage. It is a mooted question as to whether the longitudinally disposed cells lying between the elastic lamellae are muscle cells or not. In fact, in longitudinal sections, an intima of considerable thickness is sometimes suggestive of a muscular media.

We have learned to recognize therefore, two criteria of the normal productive variations in the intima, first the elastic tissue alterations, and secondly the muscular inclusion which manifests a characteristic homogeneity. If we contrast here the composition of the intima accompanying thrombotic processes, we will note the absence of muscular elements.

A third distinctive differential point between the pathological and the normal is the occurrence of alterations in the media which attend not only arteriosclerotic processes with thrombosis or calcification, but also are found in thrombo-angiitis obliterans and arteries after ligation, or the seat of embolism. These are the infiltration of the media with connective tissue, and a striking vascularization or invasion with new formed vessels, and are evidences of the participation of the vessel wall in the reactive processes incident to morbid changes affecting the intima and arterial patency.

The author¹ too, has described such morphological alterations in the media of the arteries in thrombo-angiitis obliterans, calling attention to the teleological penetration of vessels into and through the muscular coat through which they can enter or send sprouts into an occluding clot, and partake in its canalization and connective tissue transformation.

Much discussion has arisen and contentious explanations are many on the relative rôles of the media and intima in the incitement as well as actual

¹ Buerger, Proc. N. Y. Path. Soc., Feb. & March, 1908.

participation of intimal hypertrophy. The weight of evidence, as also observations of the author, strongly attest to and confirm the importance of the media and adventitia in the thickening of the intima as well as in the metamorphosis of occlusive parietal thrombi.

Jores¹ recognizes firstly an intimal enlargement in which the reduplication of elastic fibers has its origin in the existing lamellae, and secondly, a form in which proliferation by virtue of agencies acting from without (media and adventitia) inward are potent. Views are divergent as to whether the activating factor in the latter is of inflammatory nature or not.

As for the source of the new formed elastic fibers, contradictory expressions of opinion are found amongst pathologists. Whilst Jores assumes that new formed elastic fibers must emanate in the first type (which he calls hyperplastic thickening of the intima) from the internal elastica, and in the second form (to which he applies the term "regenerative proliferation") from prolongation and hyperplasia of existing elastic fibers of the media, and, whilst he desires to controvert the theory of metaplasia from connective tissue as a mode of production of such tissue, the author has shown that so restricted a view is untenable. For, newly formed elastic fibers appear around and encircle the new vessels in the center of the organized occlusive thrombus, at situations widely removed, and in no sense continuous with similar fibers of the media or intima. Such neoplastic vessels, it is true, arise from new formed capillaries that may represent prolongations from similar structures in the media, but the elastic fibers about them could not have been carried in by the angioblasts from which the older vessels were born and had matured. This special perivascular distribution in the author's opinion, speaks in favor of the following view: That elastic tissue fibrils are made out of the collagenous connective tissue elements (metaplasia?) by a stimulus derived from the endothelial cells; and that that impulse bears a direct relation in intensity, to the intravascular carrying power of the vessel enclosed by the new formed lamellae; that the endothelial cells themselves do not produce elastic tissue is fairly certain, but that they predetermine the elaboration and distribution of such tissue is more than likely. The older and larger the new vessels in the thrombus of thrombo-angiitis obliterans, the more elastic elements are formed.

Although this view is not in accord with that of Jores, it finds adequate support in the abundant material elsewhere described (Chaps. LXI and LXII). That this author's concept of the varied arterial lesions is limited by lack of experience with that most instructive form, thrombo-angiitis obliterans, is confirmed by his own words. In the passages on arterial lesions of "spontaneous gangrene," he says: "Ueber diese Erkrankung stehen mir eigene Beobachtungen nicht zur Verfügung" ("I have made no personal observations on this disease"). From his perusal of the literature, which we have elsewhere demonstrated to contain fallacious and misleading interpretations, Jores concludes that the lesions are to be grouped under his form of "regenerative hyperplasia."

In *arteriosclerotic* vessels, Jores recognized both varieties of intimal change, the purely hyperplastic with not only reduplication by cleavage, but also by true proliferation; and the second type of regenerative connective tissue growth in the intima, or combinations of the two. Often the separated elastic lamellae enclose new formed connective tissue which may include foci of degeneration.²

Jores emphasizes the importance of the finding of two histologically separable and diverse types of intimal change, postulating for these different causal agencies. Such a view he holds to be contradictory to the accepted³ uniformity of explanation for the vascular lesions in this disease.

The theory that inflammation is responsible he considers untenable, since the typical hyperplastic manifestations occur in normal arteries, are seen in children and are unaccompanied by any of the usual histological structural elements of inflammatory processes. Since this type of intimal thickening is the predominant one in arteriosclerosis, the inflammatory theory is incompatible with the appearances described by the afore-mentioned.

The Hyperplastic Intima.—As for origin of the type with cleavage of elastic lamellae, two hypotheses may be entertained. Firstly, we may regard the overgrowth of the intima as a physiological response, and that this proc-

¹ Jores, *Loc. cit.*

² That this view is incorrect, the author's researches on thrombo-angiitis obliterans have conclusively demonstrated.

³ That is, up to the year 1903 when the monograph of Jores appeared.

ess extends itself in arteriosclerosis, becomes more intense, suffers attendant fatty degeneration and connective tissue infiltration.

Secondly, a non-physiological basis may be considered. One may suppose that there are noxious influences that are present to a greater or less degree in all persons, causing intravascular lesions in certain of them with the aid of other predisposing factors. The irregularity of the distribution of the foci of intimal hyperplasia in the very young and the absence of such a change in the embryo would speak in favor of such a view. Then, too, the gradual transition into the degree considered pathological is of moment.

Such an injurious element leading to hypertrophy of the intima is in all probability an increased functional burden or augmentation of the normal intravascular pressure. If we consider that there is often a distinct quantitative relationship between the hypertrophy of the longitudinal muscular fibers and the thickening of the intima, this theory obtains additional support.

According to Fuchs,¹ amongst the developmental irritants for the vascular wall, that is, of the factors influencing growth, a periodic, physiologic, rhythmic impulse is important. An increase in pulse tension is to be regarded as such. If we transfer this hypothesis to the conditions in which the physiological passes over into the pathological, we can assume that both hyperplasia of the intima, as well as the longitudinal musculature can follow in proportion to the degree of abnormal physiological irritants.

Genesis of the Regenerative Connective Tissue Proliferation of the Intima.—There is no doubt but that connective tissue growth in the intima may be associated with or without inflammatory processes. In arteriosclerosis both lesions of intima and media with their concomitant fibroses would seem to owe their existence to some other than an inflammatory motivating agent.

The researches led Jores to conclude that hypertrophy of the intima precedes the arteriosclerotic process, which in the aorta is comparable to the hyperplasia of the first years of extrauterine life and is attended with hypertrophy of the musculo-elastic longitudinal layers.

The hypertrophic intima with the musculo-elastic longitudinal layers, tends to undergo fatty degeneration. As a result there follows a proliferation of connective tissue which may be diffuse or circumscribed depending on the extent of the degenerative foci. Since all diffuse fibroses of the intima are not of arteriosclerotic nature, and since a diffuse endarteritis fibrosa whose causation and significance are still unknown, can occur, other characteristics must be sought to differentiate and stigmatize the *arteriosclerotic* lesion. Such are the participation of a hyperplastic intimal layer with fatty metamorphosis of the latter, and the development of a connective tissue ground substance between the elastic lamellae.

An increased functional demand on the arterial wall seems to be the *sine qua non* for the origin of the *arteriosclerotic* process. In respect to the nature of this change from the normal physiological, intravascular, mechanical and hydrostatic conditions, heightened blood pressure with its concomitant increased tension of the vessel wall would seem to offer the most satisfactory explanation. Whatever impresses itself upon and especially influences longitudinal musculo-elastic layers of the vessel wall to an excessive degree, would be the most probable motivating agent in the calling forth of structural responses, manifested as "*arteriosclerotic*."

Experiments in which the intracanalicular pressure in rubber tubing or a hose is altered, give valuable information for deduction. Let us inject or

¹ Fuchs, R. F., Zur Physiologie u. Wachstums Mechanik des Blutgefäß-systems. Habilitationsschrift, Jena, 1902.

force into an elastic tube an increased amount of fluid. We will find that not only will the tension increase, but a lengthening will take place, showing itself in a motion of the whole tube. In the arteries the circular muscular coat whilst in a state of tonicity or contraction, easily limits the expansile increase of pressure (felt as pulse), whilst the mechanically more restricted action of the longitudinal fibers permits of considerable elongation of any given arterial length. This manifestation is clinically observable in the tortuous temporal arteries. In these an elongation with increasing age and a serpentine motion transmitted by each heart beat are well known phenomena.

Excessive pressure then would seem to make even greater demands in the longitudinal elements than on the relatively stronger circular ones; and consequent reactive hypertrophic changes characterized as arteriosclerotic would be the vascular response.

Experimental Arteriosclerosis.—Because the arteries are under the influence of so many varied factors, partly hydrostatic, partly pulsatile forces and constantly changing intravascular stresses, and since they are subject to the chemical influences of the blood (toxic and bacterial)—the possible components making for pathologic alterations are indeed many. Considerable experimental work has been done in animals with a view to reproducing some of the pathologic alterations seen in the human, particularly the athero- and arteriosclerotic. It may suffice here to recount in brief some of this work, in order to point out the manner in which possible etiologic factors should be interpreted.

In the attempt to produce arteriosclerotic changes most experimental work has failed, in that an exact reproduction of the typical alteration has not been possible. However, interesting results followed the administration of adrenalin products in animals. It has been possible to bring about distinct changes in the arteries. Most of the authors agree with the findings of Josué.¹ The changes comprise whitish areas and granular changes in the intima of the aorta; streaks and larger areas of thickening of the same region, with precocious calcification; discrete or confluent lesions, with partial umbilication; and aneurysm formation of varying size up to that of a bean. The lesions vary in size from microscopic up to plaques about 0.5 cm. in diameter.

Microscopically it was found that a primary change occurred in the media, particularly in its central two-thirds. This is said to be typical, extending in plaque-like fashion through the muscular coat, and on cross section appearing as small streaks or segments of a circle.

The muscle cells show their degeneration in the loss of tinctorial properties, fragmentation and loss of their nuclei. Most investigators admit that a necrosis of the muscle cells occurs.

Klotz² mentions that fatty degeneration of the muscles is regularly initiated by adrenalin injection. According to his view neutral fat is first formed; this is converted into fatty acids, and these later produce insoluble soaps with the calcium of the blood and lymph.

Saltykow³ on the other hand, regards the fatty conversion to be inconsequential, the essential process being the necrosis.

The elastic elements are said to undergo characteristic changes. The lamellæ in the neighborhood of the foci lose their undulatory course, approach each other and seem to become somewhat agglutinated. Others (Külbs⁴) speak of a separation of the elastic fibers. The lamellæ show granules, stain poorly, may tear, become fragmented or split. Finally they undergo degeneration and may disappear. Klotz refers to such degenera-

¹ Josué, Presse méd., 1904, S. 281.

² Klotz, Jour. Exper. Med., 1906, 8, p. 322; also p. 504.

³ Saltykow, Centralbl. f. allg. Path. u. path. Anat., 1908, XIX, p. 321.

⁴ Külbs, Verhandl. d. XXII deutsch. Kong. f. inn. Med., 1905, p. 246.

tion. Calcification is an early process; sometimes the specific foci are visible only microscopically.

The Intima.—Proliferation of the endothelium is mentioned by Külbs and Saltykow; others speak of degeneration of the endothelium; and still others regard the intima as thickened with normal endothelial cells covering it (Scheidemandel). The changes in the intima may precede those in the media (Papadea¹). Ziegler interprets the irregularities of the inner surface of the arteries as due to hypertrophy of the intima.

The Adventitia and Vasa Vasorum.—Changes in the adventitia are either absent or may be of a reactive nature, with perivascular infiltration. According to Orłowsky² the chief changes in the arteries are due to an obliterating endarteritis of the vasa vasorum; and others recognize a similar process with complicating hyalin thrombosis (Trachtenberg³).

Summary.—The essential changes in adrenalin atherosclerosis seem to be in the media, and the thickening of the intima is secondary. Perhaps the latter is a compensatory or reparatory process due to the weakness of the media. Opinions differ as to whether the primary changes occur in the muscle cells or in the elastic element. The weight of evidence leans towards the view that the muscle cells are first implicated, although a number of authors lean to the other contention that the elastic elements are first damaged.

As *cause* of the arterial changes a number of different explanations are given comprising the following: Increased blood pressure due to the action of the adrenalin extract; a direct elective toxic action upon the muscle elements of the media and closure of the vasa vasorum, with secondary trophic derangements of the media; or a combination of both causes.

The Relation of Human and Experimental Atherosclerosis.—Critical and comparative investigations by a number of authors have led to the conclusion that changes in the arteries of the rabbit due to adrenalin experiments, show characteristic differences from those lesions of human atherosclerosis. Distinctive features in the human are the essential localization in the intima, the degree of fatty degeneration and the subsequent calcification, as the final stage of the regressive process. In the experimental rabbit, on the other hand, there has been noted the special localization in the media, a relatively small degree or absent fatty degeneration, and calcification at the very inception of the disease.

It is still a mooted question as to whether the alterations following adrenalin injection are attributable to a specific toxic action, or indirectly through the increased pressure occasioned. That a direct action may play a rôle, has not as yet been controverted.

Experiments with nicotin and tobacco have not been convincing; and, although authors report lesions similar to those produced by adrenalin, the resemblances between the artificial and the human lesions are not sufficient to permit of positive conclusions.

Experiments have also been made with various chemical substances and bacteria. The injection of the latter has not resulted in the formation of arteriosclerotic changes. Saltykow and Klotz, however, report changes not unlike those of human atherosclerosis after injection of micro-organisms (staphylococci and streptococci). The lesions were found in the aorta and included fatty degeneration, proliferation and degeneration of the subendothelial layers. In Saltykow's rabbits the degenerative changes were so marked that he speaks of them as being easily mistaken for the human arteriosclerotic processes.

Localization of Arteriosclerosis.—The localized incidence of arteriosclerosis as it invades the arterial tree accounts for the frequent clinical confinement of manifestations to the extremities. The factors productive of the lesions are variable in that the stresses in the members include a number of different concomitant agencies. To what extent each of the determinants, such as static influences, motion, locomotion, the special affinities of toxins, and others, contribute, cannot be accurately ascertained.

¹ Papadea, Riv. di patol. nerv., 1906, Vol. II, fasc. 5. (cit. by Tarantini in Policlinico, 1906, Sez. med., Vol. XIII, p. 311).

² Orłowsky, Russk. Vrach., 1905, p. 1443; also 1907, p. 364.

³ Trachtenberg, Charkower med. Jour., 1907, III p. 468.

Concerning the sequence and frequency in which this process affects the arteries, there seems to be little or no unanimity of opinion. The order given by Albutt based upon statistics of Thoma's material is: ulnar (94 per cent), anterior tibial (93 per cent), subclavian (88 per cent), cerebral (87 per cent), internal carotid (87 per cent), radial (86 per cent), splenic (82 per cent), popliteal (79 per cent), axillary (71 per cent), femoral (87 per cent), common carotid (68 per cent), ascending aorta (67 per cent), abdominal aorta (64 per cent), external iliac (58 per cent), and brachial (55 per cent).

As far as the arteries of the extremities are concerned, the same partial, quite unaccountable distribution of hypertrophic and degenerative changes that are met with throughout the rest of the vascular system, seems to obtain. In defective metabolism, however, as in diabetes, the degenerative and calcific varieties tend to be more intensely and diffusely present. The degree and site of involvement of the several arteries of a limb, too, follow no known laws. Sometimes we glean the impression that the popliteal, especially at its bifurcation, and the distal parts of the arteries and posterior tibial are localities of predilection, only to be surprised at their relative integrity in other cases.

CHAPTER LXVIII

ARTERIOSCLEROSIS—MINUTE PATHOLOGY

For a comprehension of the organic alterations responsible for the circulatory affections and gangrene of arteriosclerotic nature, it will suffice to discuss merely those arterial lesions that are sufficiently advanced to bring about nutritional disturbances. And so we give but passing mention to those well-known early changes in which the intima alone is but slightly involved. In the chapter on the architecture of the normal arteries, it was pointed out that limited hypertrophies of the intima begin at a very early age. In Fig. 129 a minute patch of intimal hypertrophy is well depicted in a normal anterior tibial vein. More pronounced are the lesions in Fig. 130, macroscopically apparently "normal" external plantar artery, where thickening of the intima and hyalin change are easily discernible. The intermediate alterations from these minimal ones to the exceedingly destructive processes are so well known as to require no detailed description. We shall confine ourselves to an exposition of those personal observations on arteries dissected out from amputated limbs, in which the lesions were responsible for trophic disorders and gangrene.

The larger arteries in arteriosclerosis are not infrequently narrowed by the presence of a glassy gelatinous-like tissue of bluish pearly and yellowish appearance, arising from the inner wall of the vessel.

On section through such arteries this is seen to be made up of altered clot, or of proliferated intima with secondary degenerative changes. In thromboangiitis obliterans we rarely meet with such regressive phenomena in the occluding tissue, the latter being better nourished, both by reason of the number of vascular elements, and also because the nutritional conditions are far better in vessels of younger people.

Characteristic of the disease of the larger arteries is the production of a layer of new-formed tissue (crescentic on cross section), poor in capillaries and rich in hyalin connective tissue. Two types are met with; one in which the

cells are abundant and in microscopic sections give the tissue an appearance simulating unaltered young cartilage; and another form, in which the active tissue shows small compressed spaces containing distorted fixed or endothelial cells, pigment and degenerate nuclei. In such tissues as these, by reason of a sort of myxomatous degeneration, a gelatinous macroscopic product is elabor-

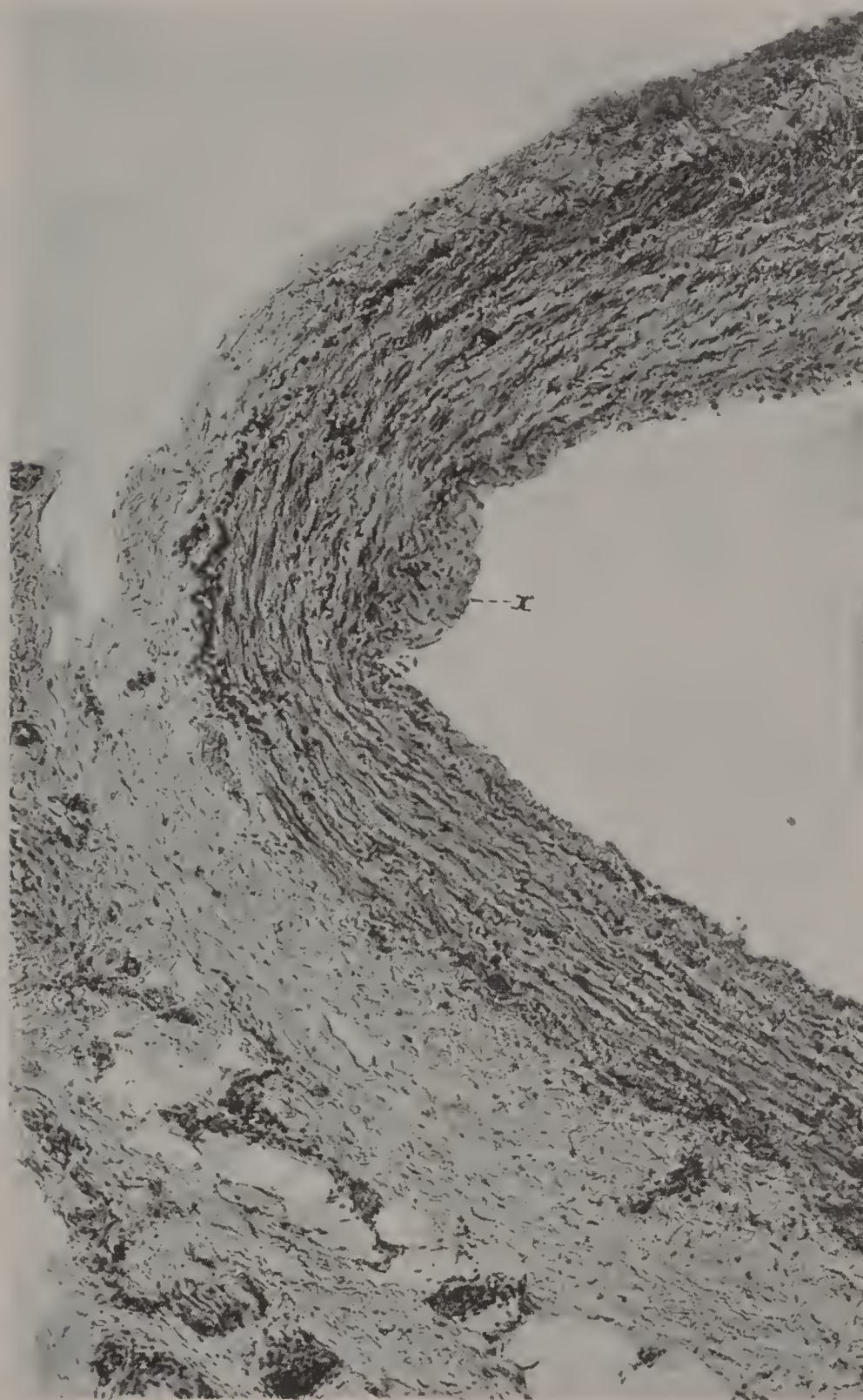


FIG. 129.—A portion of a normal anterior tibial vein showing a small focus of hypertrophy of the intima (x).

ated. Near the media, vascular spaces are frequently formed, lined with endothelium, these being the dilated remnants of new-formed vessels that have penetrated and vascularized the tissues. In addition to the previously mentioned regressive changes fatty degeneration and atheroma also take place.

Organized clot also may contribute to the formation of the glassy gelatinous looking material seen in such arteries. The clot becomes organized in typical fashion; with this process penetration with new-formed vessels and

proliferation of capillaries takes place. Later degeneration of myxomatous and hyalin variety sets in.

The obliterative lesions and the vascular lesions are well shown in Figs. 131 and 132 where the popliteal artery is the seat of typical atherosclerotic lesions with some calcification and complete occlusion, atheromatous material and intimal thickening. A reference to Fig. 131 will make clear the usual type of reduplication of the internal elastica, and the extent of the thickening of the intima, and will also show a recently organized clot whose architecture is totally different from that of thrombo-angiitis obliterans.

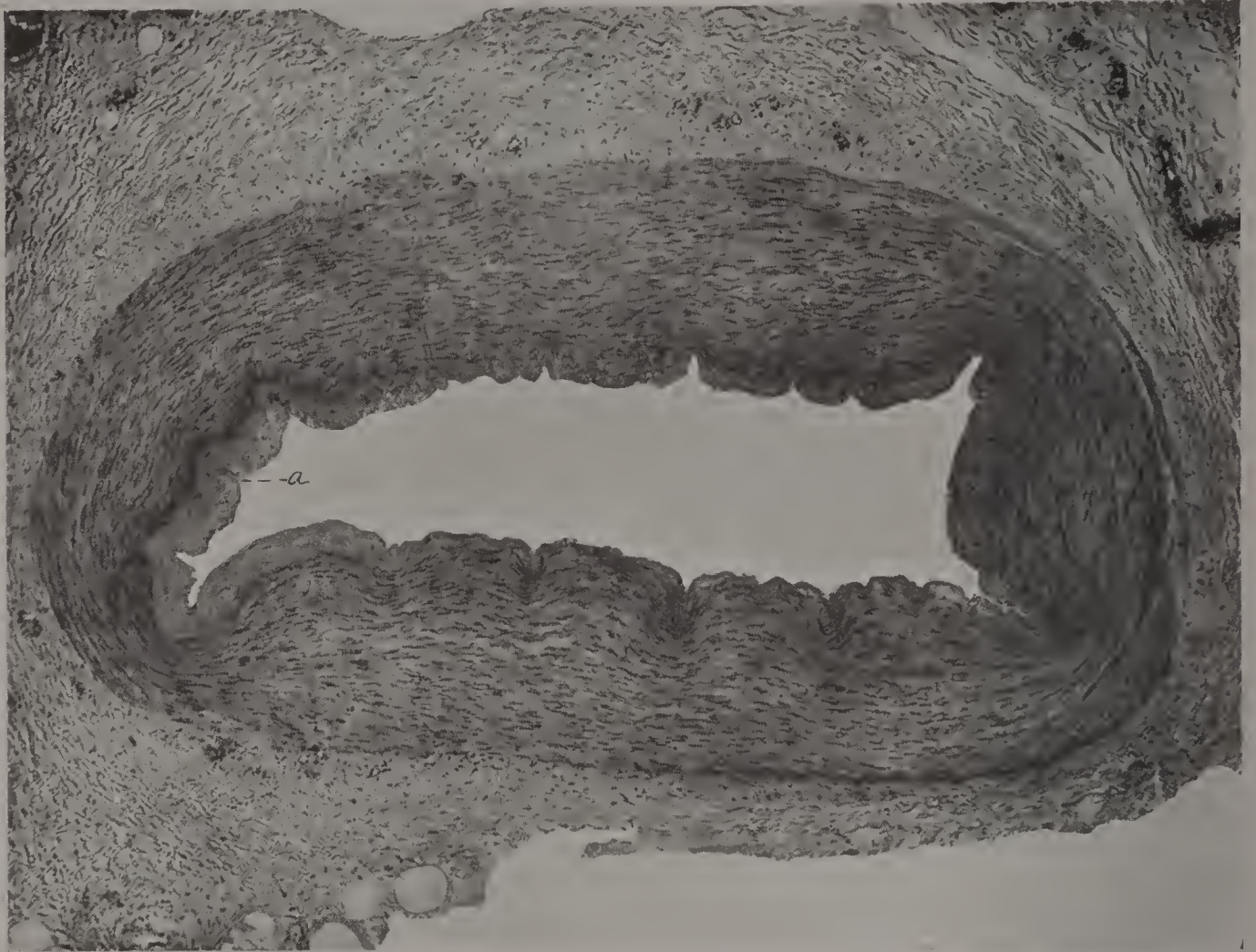


FIG. 130.—“Normal” external plantar artery with but slight hypertrophy of the intima (*a*); early lesions of atherosclerosis.

The paucity of lesions in the adventitia is diagnostic for arteriosclerosis. There is no cellular infiltration, no thickening and no adhesion between it and the surrounding structures.

In the media the inflammatory and productive lesions of thrombo-angiitis obliterans are absent, but characteristic are the lime deposits and the degeneration of the musculature. In Fig. 133 elastic tissue stains show clearly that the normal course of the circular elastic fibres is interrupted by lime deposits, atheroma, and even bone formation.

The enormous thickening of the intima with the formation of characteristic plaques is seen in Fig. 132 (*b*). Here there is a concomitant production of elastic elements, the tissue having no relation to the clot, but being the product of a proliferative process. This in places shows the typical degenerative phenomena—cellular and connective tissue degeneration with atheroma.

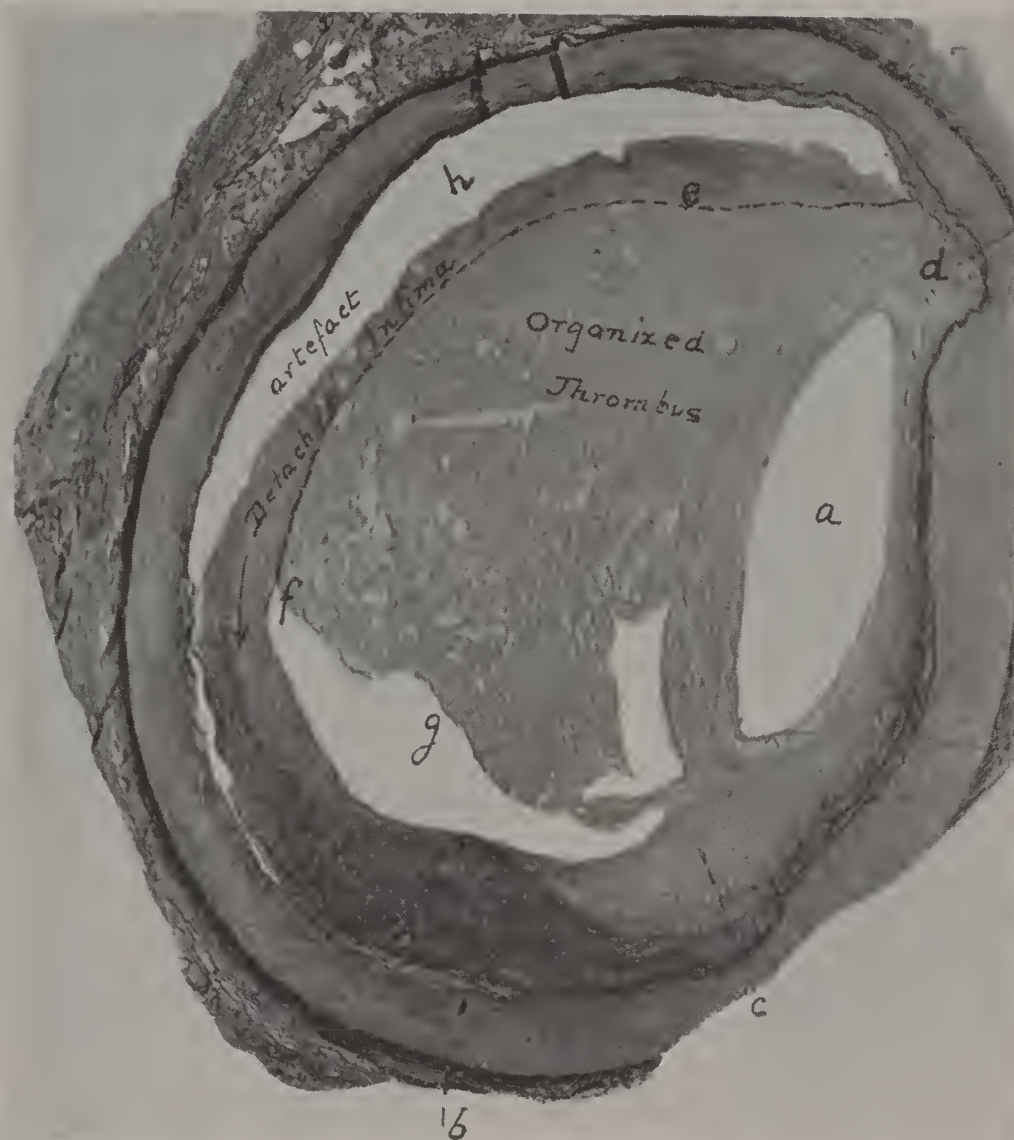


FIG. 131.—The difference in healing properties of the hypertrophied intima detached above (at *h*) and the organized clot can be appreciated in the greater darkness of the former; the loss of tinctorial properties of the degenerate intima at *c* as compared with the portion at *b* is well shown. At *h* the hypertrophic intima between *h* and the dotted line *e-f* has been detached artificially, and fuses in the picture with the organized clot.



FIG. 132.—High power of the region *b* and *c* of the artery previously shown; at *b* the markedly hypertrophied intima; at *c* undergoing myxomatous degeneration, the clot probably beginning at this point where it is adherent at *j*.

The obturating tissue depicted in the figures will demonstrate the differences between the occluding tissue characteristic of arteriosclerosis and that of thrombo-angiitis obliterans, and that the obturating tissue, as here exemplified, is composed of degenerative hyalin or myxomatous fibrillar variety in which the vascular elements are scarce or absent, plus the fused partly organized, partly degenerate thrombus.

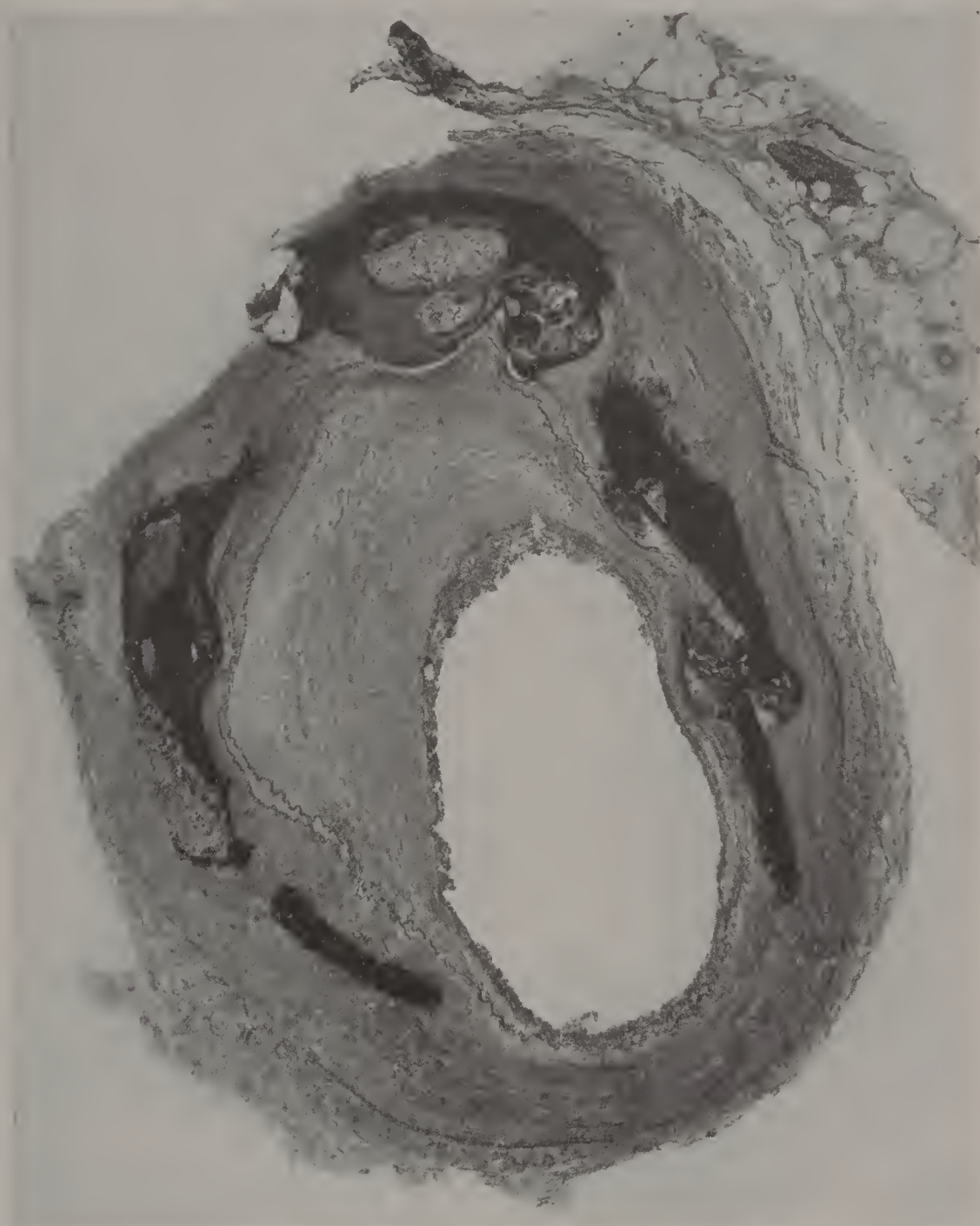


FIG. 133.—Cross section of a plantar artery in a case of arteriosclerotic gangrene.

The Larger Arteries in Gangrene. *The Obliterating Tissue.*—It is not always easy to distinguish microscopically between organized thrombus and arteriosclerotic proliferating tissue, both of which may partly or completely occlude the arterial lumen. The pearly, glassy or whitish tissue that completely fills such a lumen in atherosclerosis is most often the hyperplastic intima in a state of hyaline degeneration. The production of a peculiar hyaline tissue in which there is a rather sparse distribution of fusiform or stellate compressed cells is a characteristic feature of the obturating tissue (Figs. 134 and 135). This type of picture offers a noteworthy point of differentiation between the sclerotic connective tissue of thrombo-angiitis

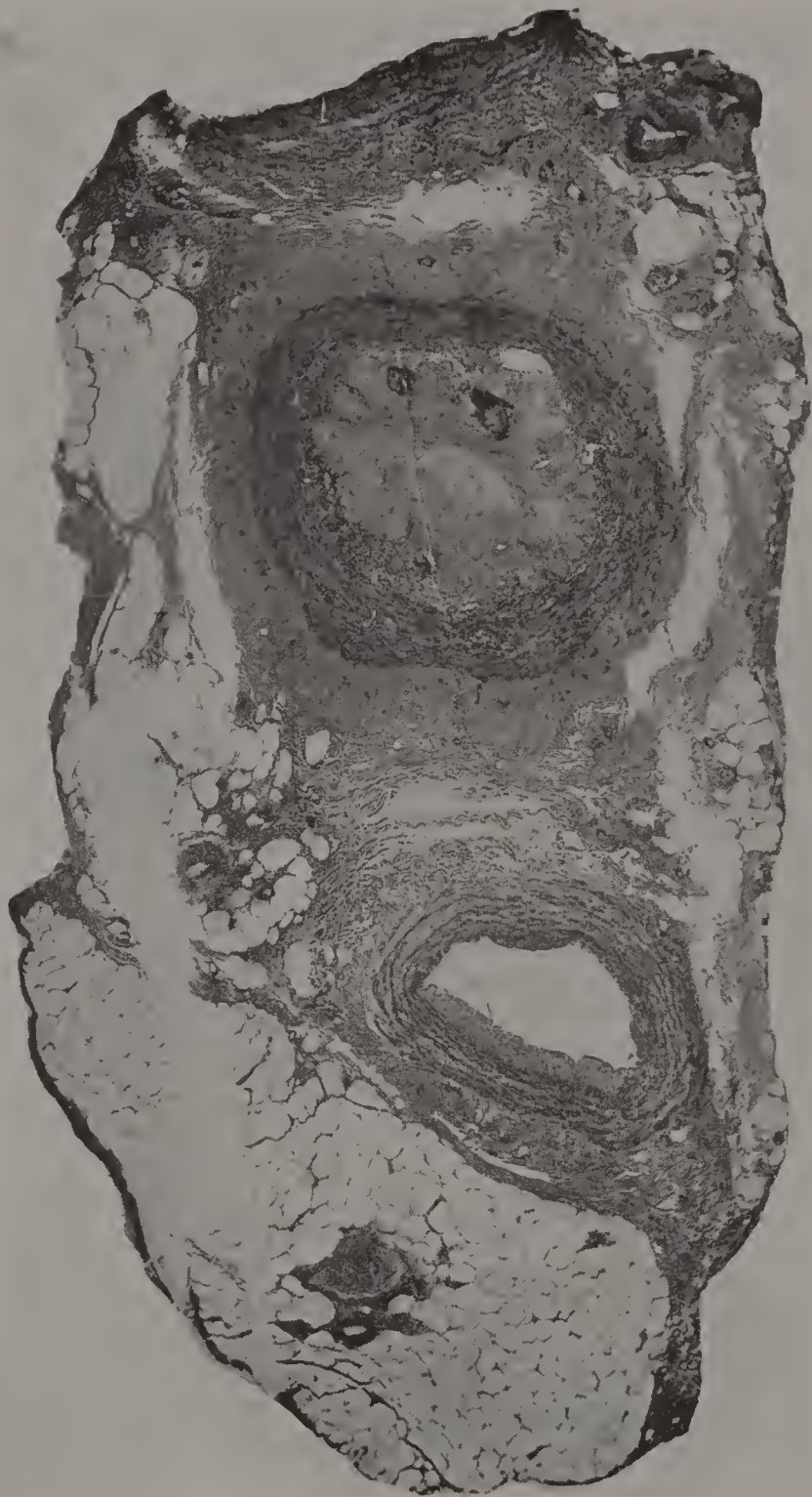


FIG. 134.—Occlusion in arteriosclerosis. The artery in the picture is closed by fibrotic tissue which is poor in cells and shows hyaline degeneration, as well as two foci of bone formation. These are seen in the dark areas, which, on magnification, would show bone cells and lime deposits. Here, too, the characteristic collections of mononuclear cells in the media without any inflammatory process in the adventitia is pathognomonic and permitting of differentiation from thrombo-angiitis obliterans. The absence of fusion of artery and vein distinguishes this from the advanced periarteritis of thrombo-angiitis.

obliterans and that of atherosclerosis. For the most part its lamellæ or pseudo-lamellæ (since these are merely separated by cells) are disposed more or less concentrically, but variations occur. Their course may be longitudinal, and cross sections of bundles are thereby obtained. It is, however, in the neighborhood of canalizing vessels that a distinct interruption of the general monotony of this picture is produced, for here the connective tissue



FIG. 135.—Completely obliterated dorsalis pedis artery (part of cross section) in a case of atherosclerosis with diabetes and gangrene. Lumen completely filled with characteristic proliferative intima, fibers of which run longitudinally or roughly concentrically; below, lime deposits and bone formation just under the internal elastic lamina; above, and elsewhere in the media perivascular and intermuscular collection of round cells; dilated capillaries, spaces, and sinuses in the media (high power of a part of Fig. 134).

fibers are often disposed in longitudinal fashion about the new-formed vessels, so that larger and smaller punctuate areas representing fibers transversely cut distinctly modify the general tone of the picture (Fig. 135).

Often the lumen is filled with connective tissue of less dense structure, containing pigment, whenever organization of a clot has taken place. Thus pictures resembling the old obliterative process of thrombo-angiitis may be

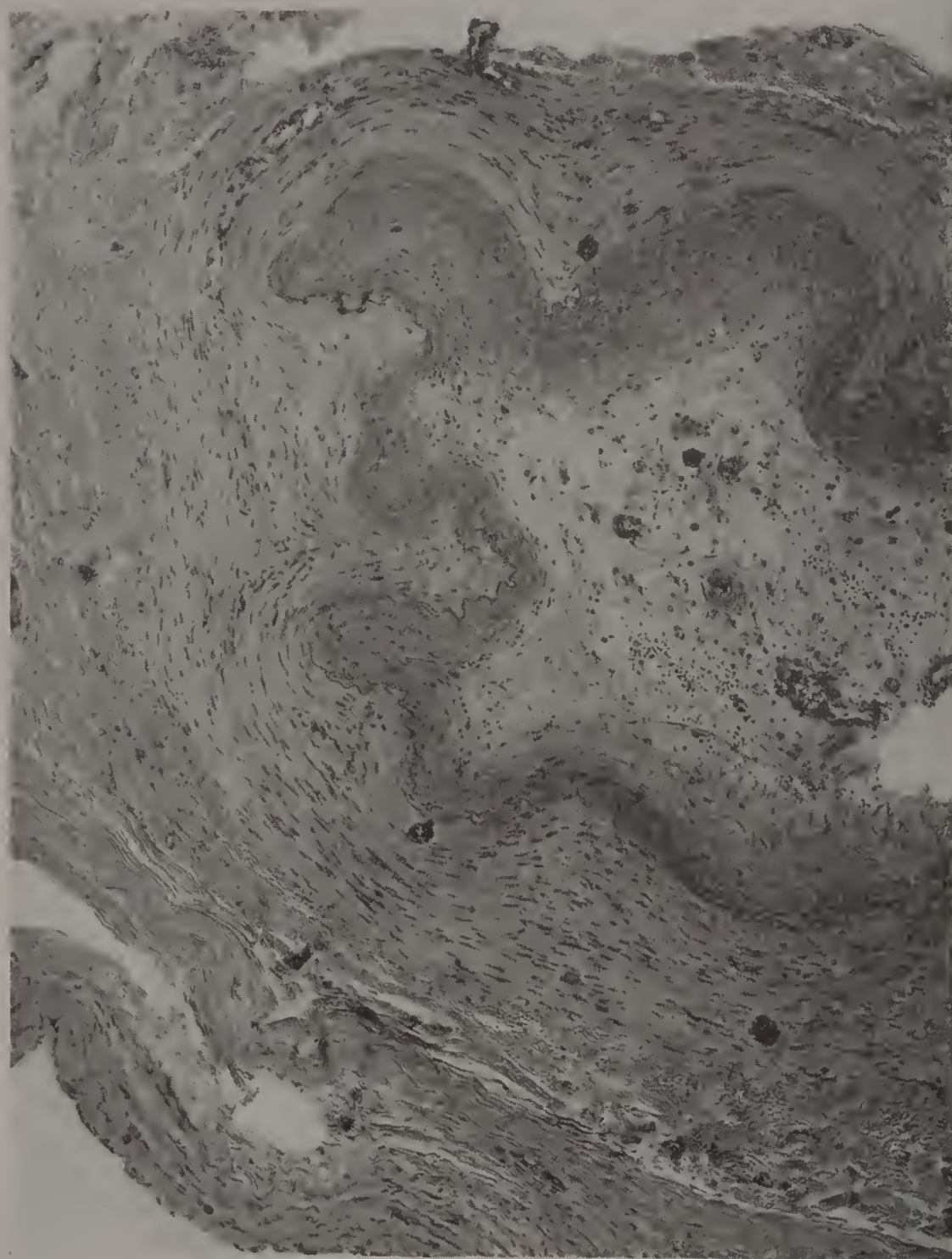


FIG. 136.—Complete occlusion through organizing connective tissue of an atherosclerotic artery; areas of calcification along the internal elastic membrane, thickening of the intima, loose connective tissue occupying the lumen.

produced (Figs. 136 and 137). The intensive elastic tissue production sometimes seen in arteriosclerosis is well shown in Fig. 138.

Recent Occlusion of Atherosclerotic Popliteal Artery.—The clinical manifestations of sudden occlusion of the popliteal artery as a complication sometimes precipitating gangrene are described elsewhere (Chap. LXIX). Mechanical or stagnation thrombi are not uncommon in arteries that are more or less stenosed and partly occluded by hypertrophic intima. The intima usually has undergone considerable hyaline or myxomatous change

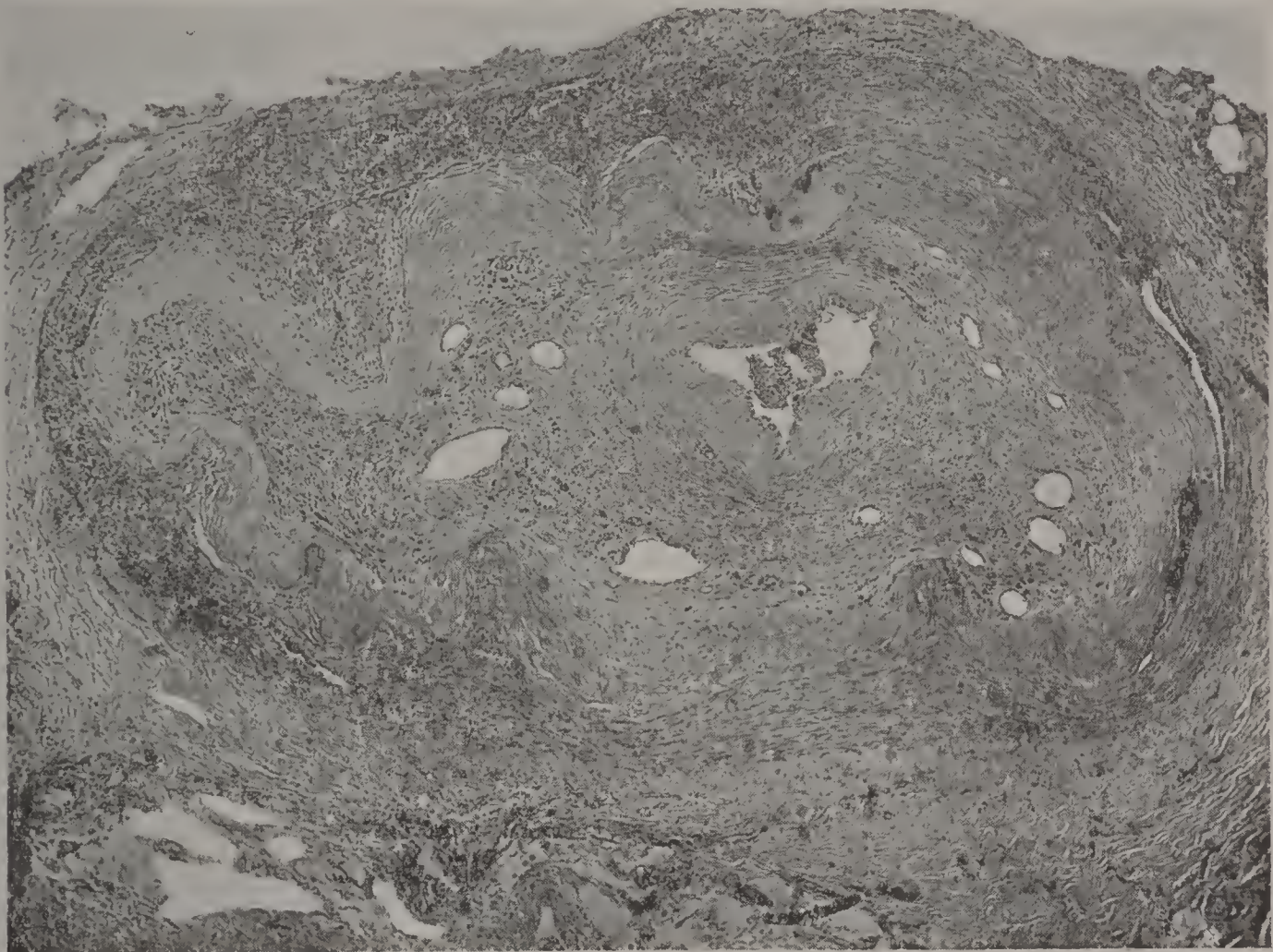


FIG. 137.—Low power of the completely occluded dorsalis pedis artery in a case of arteriosclerosis. The lumen is filled with organized thrombus and large new-formed vessels. The media above shows infiltration with mononuclears and numerous lime deposits in places. The intima is thickened in typical fashion.

with secondary atheromatous and lime deposits. Cholesterin and foreign body giant cells are not infrequently seen. The media also shows regressive changes, and in addition is characterized in the longitudinal sections of the arteries by the presence of numerous dilated vessel spaces, that doubtlessly represent an intramural collateral circulation, if such a term may be employed in this sense. A reference to Figs. 139 and 140 will show recent thrombosis in the popliteal artery. In Fig. 139 a cross section shows complete occlusion by clot; and Fig. 140 shows a longitudinal section of the popliteal artery, with distal termination of the clot.

The Media in the Obliterated Arteries.—For purposes of differentiating this disease from thrombo-angiitis obliterans, some knowledge as to the picture presented by the media at various stages of the atherosclerotic and obliterated process should be well understood. The changes are degenera-

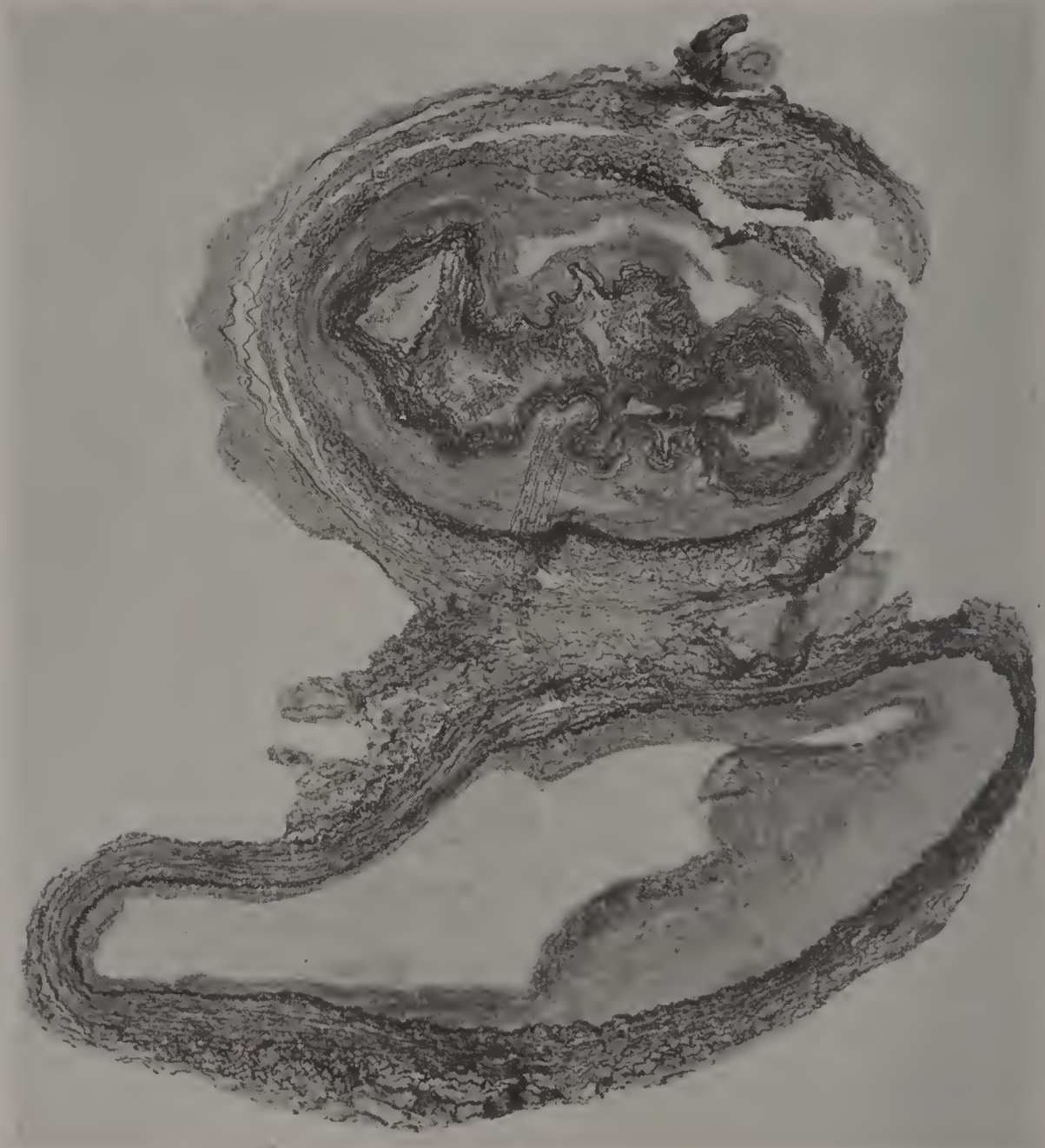


FIG. 138.—Arteriosclerotic lesion in a vein and artery. The typical proliferation of elastica in arteriosclerosis is shown, as well as the splitting of the internal elastic laminae. The absence of perivascular inflammation is also seen, and the large vein shows marked endophlebitis, the intima being markedly thickened so as to occlude about one-third of the lumen.

tion of muscle, and at the boundary between the media and intima, atrophy, disappearance of muscular elements, calcification, bone formation, cellular infiltration and vascularization.

Media Lesions when the Lumen is Filled.—When the media itself is free of lime deposit or larger degenerative processes and fatty deposits, the reactive responses due to the changes within the lumen find their best expression. The striking alterations are the areas of cellular infiltrations and the new-formed vessels.



FIG. 139.—Recent thrombotic occlusion of the popliteal artery. The media shows bone formation, calcification and the usual regressive changes; so also the typical hypertrophic and degenerative changes are present in the intima.

Just under the internal elastic lamina, we sometimes see collections of small round cells that often have a perivascular distribution in that a small capillary or arteriole is found within their midst (Figs. 134 and 135). Such foci can be traced extending in rows of cells between the more centrally placed muscle fibers of the media, and separating these considerably. Often such areas correspond to rather extensive infiltration of similar nature throughout the central half or more of the muscular layer, where longitudinally or obliquely penetrating capillaries also invade the media. In general the appearances here described are those of small foci of lymphoid cells.

In addition there may be an increased number of migrating cells scattered here and there throughout the middle coat. The vascular changes in the media are prone to strike the eye as unusual. An abnormally large number

of capillaries or even sinuses occupies the central layers of the media, some traceable for a considerable distance in a circular direction, others found to connect with vessels traversing obliquely through the media and into the adventitia; and still others, in direct communication with blood sinuses of varying size just under the internal elastic coat. The varying sizes of these capillaries and the sinuses with which they communicate give the impression that a virtual canalization or collateral circulation through the walls of the vessels as well as into the obturating tissue can and does occur (Fig. 135).



FIG. 140.—Longitudinal section of the popliteal artery recently occluded (same as Fig. 139). The media shows numerous dilated vessel spaces (intramural collateral circulation); the intima is markedly thickened, showing degeneration, atheroma. The lumen is filled with recent clot terminating distally (below in the picture).

Although an increased vascularity of the media is not pathognomonic for arteriosclerotic processes and is present also in thrombo-angiitis obliterans, we have nevertheless, here a distinctive point of differentiation. For, the larger sinuses and the apparent attempts to form devious vascular surrogates for the lost lumen are wholly absent in thrombo-angiitis obliterans.

Because of the convoluted course of the internal elastic coat and the marked intrusion of the plicae towards the lumen of the vessel, sclerotic and obturated vessels often give a picture that is confusing. For, when foci of special character lie in the peninsular projections of the internal coat, they may project so far into the obturating mass, as to appear to lie within the latter. In truth, on closer observation we will notice that the calcific deposits, the degenerate areas and the bone formation sometimes present,

are confined to the media or lie in such prolongations. Arteries that show small areas of lime deposit in the internal coat, in and just outside of the internal elastic lamina, may often give the appearance of lime plaques within the occluding mass. However, one sees just at the internal limiting membrane a larger or smaller focus of lime deposition, often partially converted into bone or osteoid tissue (Fig. 135). It is significant, too, that immediately adjacent to, or leading up to such areas, we almost always find one or more minute vessels.

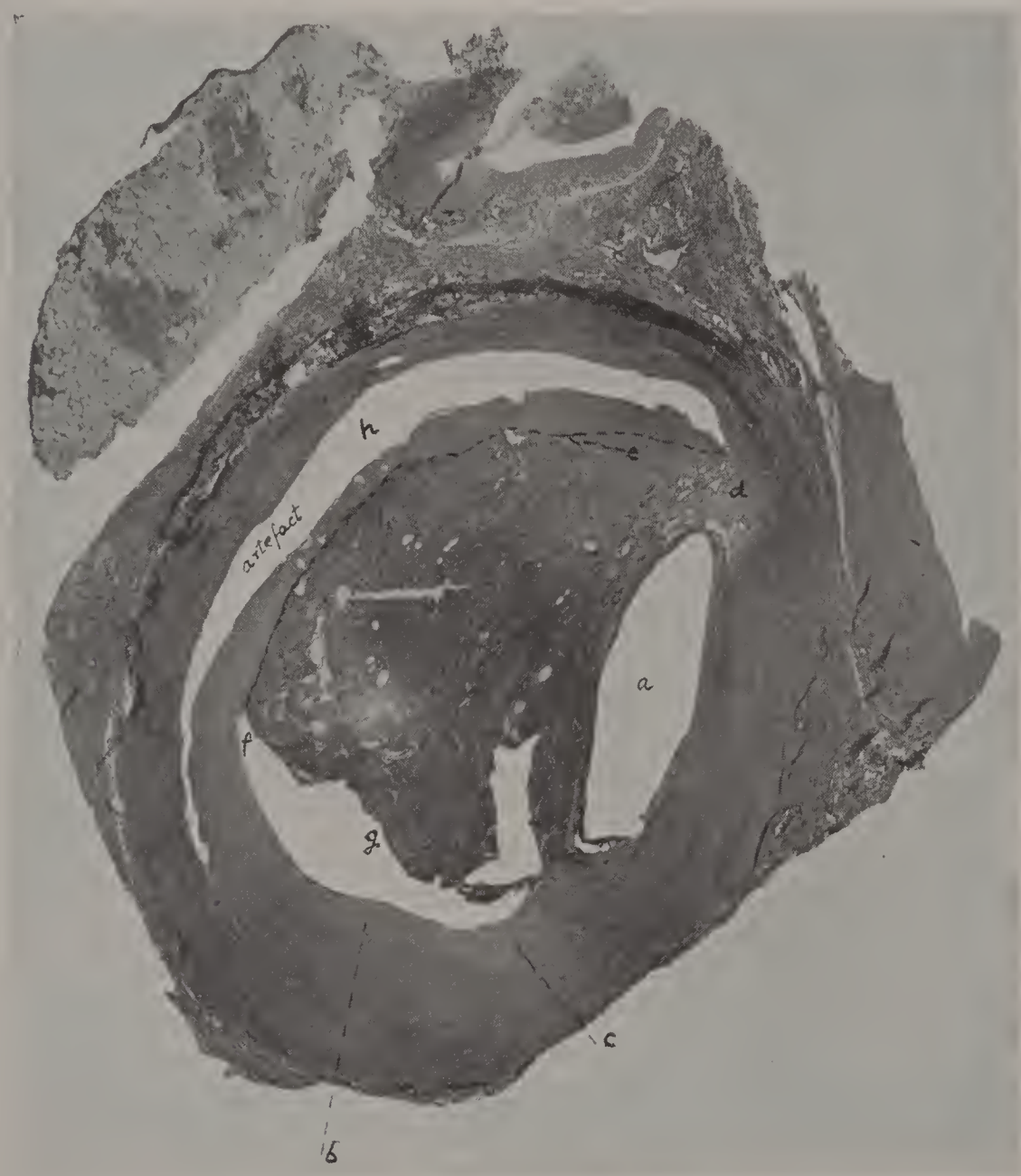


FIG. 141.—Cross section of occluded popliteal artery in atherosclerosis (same as Fig. 131). The greater part of the lumen, were it not for the artificial retraction of the obturating mass would be filled except for the roughly elliptical area of lumen left at *a*. The obturating tissue is composed of hypertrophied intima most marked at *b*, myxomatous at *c*, making a crescentic zone of firm, partly degenerate tissue. The rest of the lumen is filled by organized clot, also in state of degeneration (hyaline, myxomatous) fusing imperceptibly with degenerate intima, but distinguishable from it by the absence of elastic tissue. At *a* residual lumen; at *b* typical intima proliferation; at *c* hyaline or myxomatous degeneration of intima; *d* to *e* to *f* to *g* represents organized somewhat degenerate clot, fusing intimately with the detached intima along the line *ef*.

Arteriosclerosis with Mixed Occlusion.—The occlusive process may be wholly due to the thickened intima and the heaping up of degenerative products. On the other hand, to the crescentic shaped¹ hypertrophy of a

¹ On cross section.

part of the wall of the intima, occlusive thrombosis may be added, and the end-products after organization, develop into a tissue of varying appearance and consistency. Sometimes it may be glassy, gelatinous, pale, greyish-white or yellowish in appearance, or possess an admixture of red areas of recent clot; or it may contain brownish firm clots that represent earlier stages of organization. We often find the peculiar gelatinous tissue in the larger arteries, such as the popliteal.

A study of most of the atherosclerotic lesions and of the occlusive thrombosis may be made from Figs. 131 and 141, taken from a popliteal artery in a case of gangrene.

The media and adventitia show the usual characteristic changes of arteriosclerosis. In the adventitia the striking features are the absence of inflammatory lesions and of perivascular fibrosis (the latter so characteristic of thrombo-angiitis).

Even a gross view of the *middle coat* reveals a noteworthy disorganization, in the varying thickness and the degenerative products. While in places it is very thin, in others the normal girth is well conserved or increased.

In those portions of the media in which but little attenuation has taken place, the nature of the process is most easily demonstrated in arteries of this sort. The degeneration of the muscle fibers, their separation by infiltrating fatty deposition, and minute granules of lime in streaks or in plaques are the significant changes. These are so well known as to require but passing mention. However, it should be borne in mind that the infiltration with lime deposit goes on so insidiously that large areas are already extensively involved before the calcareous plaques are definitely formed.

The Occluding Tissue.—As above stated this is composed of two distinct portions which may fuse so imperceptibly as to be microscopically indistinguishable except on close scrutiny, namely, the crescentic and partly annular intimal hypertrophy in its varying aspects of degeneration and the organized clot. A reference to Figs. 131 and 132 will make clear how difficult it may be except with a high power objective to clearly separate the hyalin (or myxomatous) hypertrophied intima from the organized clot that has undergone a similar regressive process.

A reference to Fig. 131, which is stained with the elastic tissue stain, however, clearly shows that even the degenerative intima takes on a sufficiency of this stain (orcein) to demonstrate its greater age, and the concentric and more or less parallel arrangement of the elastic fibrils therein.

The Intima in the Larger Vessels.—Sufficient emphasis has been laid upon the nature of these lesions in the text books to make a detailed description superfluous here. We shall, therefore, dwell only upon those minutiae that may be important for those who wish to study the relationship of the thrombotic lesion in these vessels and those in other vascular affections; and those changes shall receive attention which are at first sight confusing and difficult of recognition and differentiation from the hyalin degenerative alterations occurring in bland organizing thrombosis.

Much can be learned from a study of those larger arteries in which the pulsative and distensive stresses find their most intensively elaborated reaction in hyperplasia, as in the popliteal and femoral arteries.

The typical tissue with its peculiar cell inclusion of a hyalin nature, so characteristic of intimal thickening forms plaques of varying size, that intrude into the lumen and bring about a corresponding coarctation. While the nature of this tissue is easily recognizable under the microscope, certain portions of it, when undergoing degeneration (Fig. 132), and when the fibers

are separated by fluid infiltration, may so closely resemble the hyaline degeneration of organizing blood clots, that confusion may arise.

Elastic tissue stains, however, give the most reliable information and permit of the best differentiation between a clot and the degenerate intima. Grossly, such separation is not always possible.

If we refer to the figures, such as Fig. 132, in which the elastic fibers of the intima are brought into view, three distinctive forms are encountered; firstly, duplication of the internal elastic lamellæ; secondly, the old concentric proliferation of new elastic tissues in the hypertrophied intima; and thirdly, those sparse and irregularly disposed elastic fibers that are found in the regions of the intima that have undergone degeneration.

A reference to Figs. 132, 138 and 142 will illustrate clearly the nature of the reduplication of the internal elastic lamina in typical fashion.

In the second zone (Fig. 132 at *b*) clearly brought into view by the stain the elastic fibers are distinguished by that lack of continuity that has been previously referred to (Fig. 131). They are detached short fibrils, deposited in the intercellular substance, and therefore surround and embrace the characteristic cellular inclusions. From the intensity of the stain, however, we can adjudge that they are of considerable age, and their general conformation and interrelationship stamp them at once as a part of a new-formed intima wholly separate from the organized clot.

The third zone (Fig. 132 at *c*) may be single or multiple and comprises that portion of the intima which has undergone degeneration. A lenticular area of this hypertrophic intima is apparently of different structure, in that it stains less deeply, and has a greater affinity for the hematoxylin stain, also in the wide separation of the cells contained therein. In these a sort of hyaline or myxomatous and in part fatty degeneration takes place, with a consequent disruption of the few fibers of elastic tissue therein contained. As a result, the elastic tissue stains are much less deep, since the fibers are less numerous and broken up. It is these degenerative areas which, when fused with the organized clot, make a composite mass that might be incorrectly interpreted as having the same origin, but which belong on the one hand to the intima, on the other hand to the blood clot. The absence of the diffusely deposited elastic fibrils in the organized clot distinguish the latter (Figs. 131 and 132).

The organized clot in such vessels presents nothing unusual. However in those obturating masses of thrombotic origin that have undergone degeneration, and in which surface vascularization cannot take place by reason of the poor circulatory conditions in the vessel wall, there is a relative preponderance of myxomatous or hyaline degenerate connective tissue with rather few organizing vessels. In places the degeneration may be of a nature similar to that going on in the contiguous intima, so that the two fuse into a mass whose identity can only be cleared up through the elastic tissue stain (Figs. 131 and 132).

The peculiar hyaline thrombi give important information regarding the differences in the response of the more muscular arteries, and of the larger type of arteries, to the thrombotic processes. The lack of reactionary elastic activity and hyperplasia in the clots of the larger vessels is in keeping with the vascular and more elastic nature of the arterial wall. Wherever we are dealing with thromboses in the smaller more muscular vessels, in which easier penetration with new-formed vessels from the adventitia can take place, we find more firm connective tissue in the clot, and more rapid organization. The myxomatous and hyaline clots are characteristic of the larger vessels.

The Pathology of the Smaller Vessels.—By illustrative description of the varying lesions in the smaller vessels, much of diagnostic value can be learned, and the interpretation of pictures simulating thrombo-angiitis obliterans can be facilitated. It is when we are dealing with gangrene and in cases in which the vessels show but sparse distribution of atherosclerosis, and where the advent of gangrene seems to be attributable to extensive thrombotic closure of the popliteal, that the exact nature of obturating lesions in the peripheral vessels (plantars, dorsalis pedis, posterior tibial, etc.) may require some analytical skill. In the chapter on the Clinical Course of Arteriosclerosis

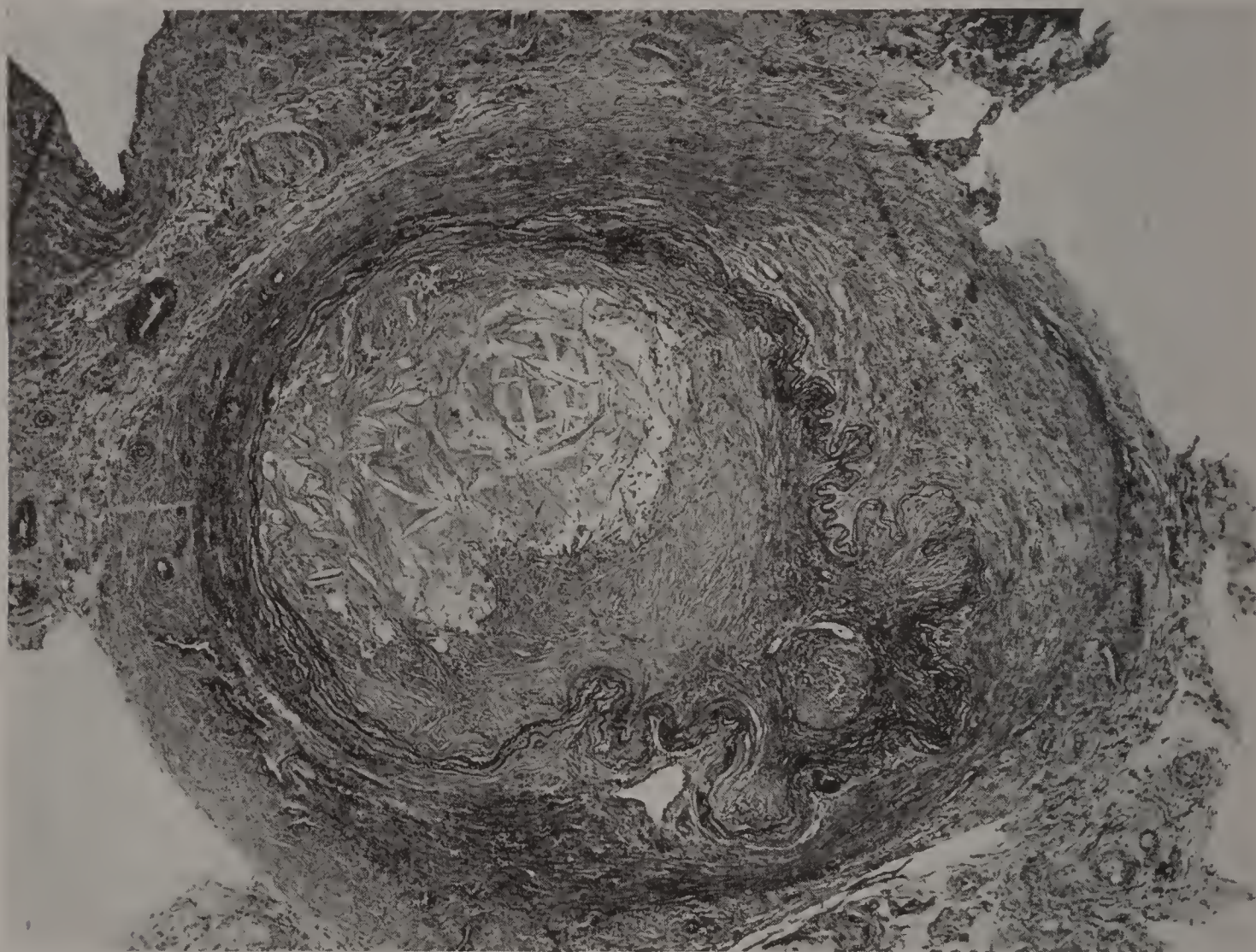


FIG. 142.—Cross section of posterior tibial artery in case of atherosclerosis. The lumen is completely filled with new-formed tissue; to the left and above, there is a large clear area with fatty degeneration, with slit-like spaces containing cholesterin crystals, two of which (needles) can be distinctly seen at about 8 or 9 o'clock as sharp black lines; the characteristic reduplication of the elastic membrane, and the absence of periarteritis and the normal separation of the vein above and to the left in the picture from the artery with no inflammatory process intervening, are well shown.

with Thrombosis the manifestations of this combination of lesions have been discussed. There we have dealt with the differentiation between chronic atherosclerosis attended with recent popliteal or femoral thrombosis on the one hand, and thrombo-angiitis obliterans with engrafted thrombotic arteriosclerosis on the other. While the recognition of bland thrombosis in the popliteal is easy when it complicates arteriosclerotic lesions, some of the older isolated obturating foci in the peripheral vessels may be more difficult of interpretation.

Although old canalized thrombi in arteriosclerotic vessels occasionally give pictures almost identical with thrombo-angiitis obliterans, except for

the associated calcific and degenerate changes in the walls, an investigation of more material will usually reveal pictures that are distinctive of arteriosclerosis.

It is the degenerative phenomena of the proliferated intima, the character of the internal elastic membrane and the regressive and degenerative changes in the subintimal layers and media that are pathognomonic for arteriosclerosis. And so, whenever a large part of the obturating tissue shows these characteristics, the diagnosis of arteriosclerosis can hardly remain in doubt. In thrombo-angiitis obliterans fatty degeneration does not take place in the obturating tissue.

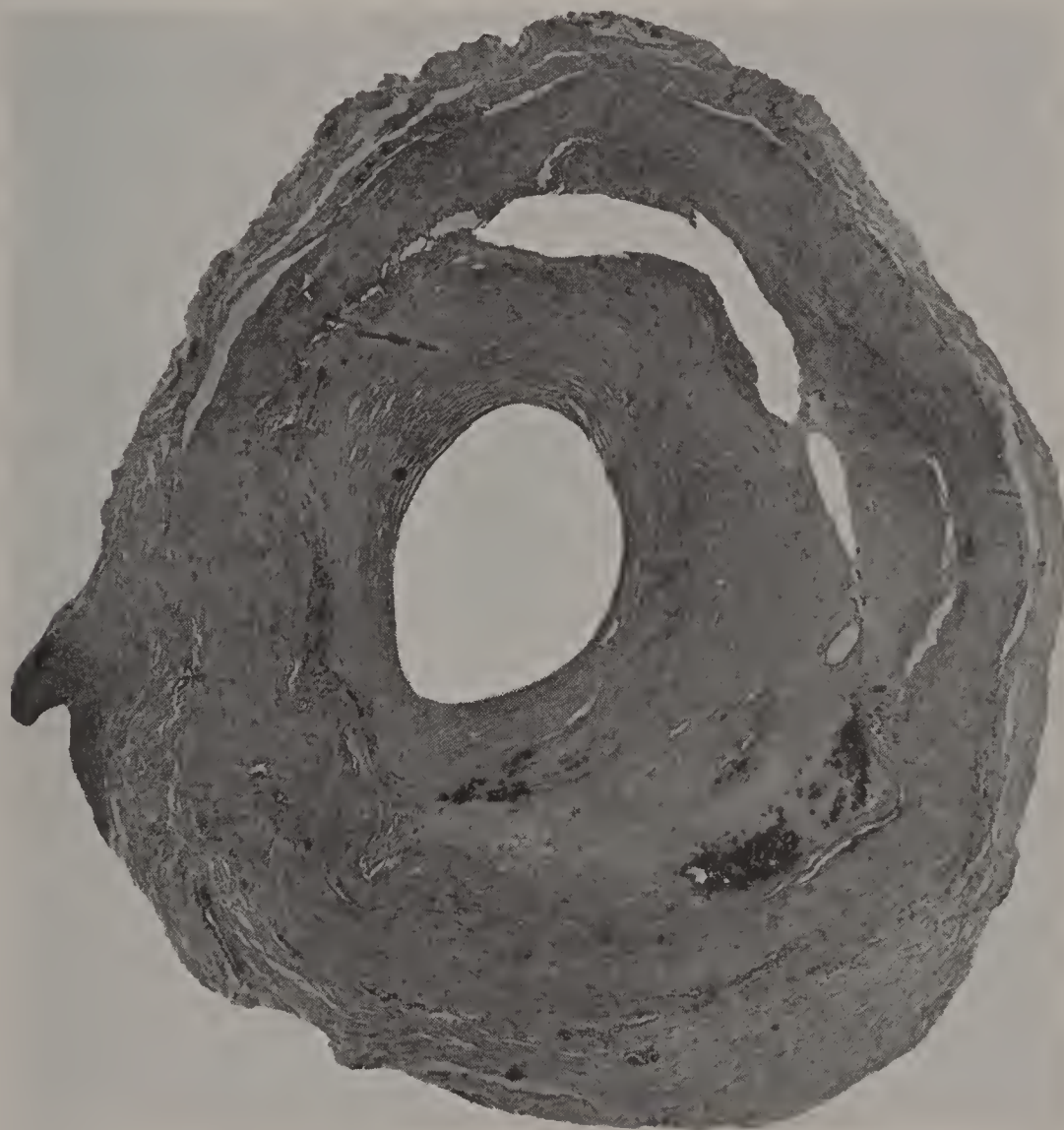


FIG. 143.—Cross section of artery of the leg in a case of arteriosclerotic and diabetic gangrene. The lumen is almost closed by onion-like concentrically and eccentrically placed proliferation of the intima, the larger ovoid space being the narrowed lumen, the longer narrower spaces being artefacts. The lime deposit in the intima, the nature of the intimal proliferation, and the absence of vascularization of the media, when thrombosis is not present, are here well demonstrated.

A reference to Fig. 142 will show a part of the posterior tibial artery in a case of atherosclerosis associated with popliteal thrombosis.¹ A large part of the occluding tissue here is made up of tissue in which there are a multitude of spaces containing cholesterol crystals. The typical retracted spaces along the margins of which the well known cholesterol giant cells are to be found in some of the sections are diagnostic of arteriosclerotic intimal degeneration. The associated regressive foci with lime deposits just under the reduplicated internal elastic laminae are also striking features. Furthermore, *the absence*

¹ See p. 423, Case S. S.

of *periarterial fibrosis* and the lack of fusion with the practically normal vein, are features belonging to the same disease.

Arteriosclerosis with Calcification.—A common type is the one illustrated in Fig. 143, where the distal part of the anterior tibial, at the junction of the dorsalis pedis depicts the ordinary concentric infringement upon the vessel lumen. The obturation originating from the walls is usually eccentric in that the mural thickening is greater at one portion than at another, giving the characteristic crescentic encroachment of the lumen seen upon section of



FIG. 144.—On the right is a muscular branch of the popliteal artery with extensive advanced calcification and bone formation (pipe-stem artery). The pale, inner layer is the zone of intimal thickening with osteoid tissue and calcification on the right. The darker band encircling the artery represents lime deposit. To the left, an accompanying vein with marked thickening of the intima, hypertrophy (phlebosclerosis).

the vessel. Such a picture would hardly give any cause for misinterpretation, since certain distinctive features are represented by it. The new-formed tissue shows a paucity of cells, the peculiar diffuse degeneration, and the deposit of lime. The last is more intense near the internal elastic lamina. The absence of periarterial fibrosis is also well illustrated here.

When the calcareous deposits are extensive—and these may affect the very smallest branches as well as the large—the well known pipe-stem arteries are formed. The process is well illustrated in Fig. 144 where the accompanying vein is the seat of marked intimal thickening (phlebosclerosis), and hypertrophy.

An even more striking picture is that presented by those specimens where there are large plaques of lime deposit and bone formation (Fig. 133 at 12 o'clock). The lenticular or crescentic hyperplasia of the intima is beautifully shown.

Bone Formation in Sclerotic Arteries.—This process is so well known, that but a few characteristic pictures need be shown here. These will demonstrate the cellular activity that accompanies both the resorption of the lime, and the conversion of connective tissue and lime into osteoid and osseous tissue (Buerger and Oppenheimer¹). The action of cells similar to those known as osteoblasts and the conversion of lime areas into bone are well shown in Figs. 133 and 145.



FIG. 145.—A small portion of the media of an atherosclerotic artery in which bone formation is depicted; above, the fibres of the media infiltrated with small round cells are seen; in the middle the dark area represents calcified material in which bone formation is going on; the central portion has been replaced by connective tissue containing small vessels and numerous round cells; the areas of bone formation are well depicted.

CHAPTER LXIX

ARTERIOSCLEROSIS WITH THROMBOSIS—CLINICAL COURSE

Arteriosclerotic Gangrene with Thrombosis.—Sudden thrombosis or extension of old thrombotic process in arteriosclerosis must be regarded as being a complication of extensive arteriosclerotic or atherosclerotic disease of the vessels of the lower extremities. If we study the pathological findings in the arteries of legs amputated for gangrene, and compare these

¹ Buerger and Oppenheimer, Jour. Exper. Med., April, 1908, Vol. X, 3.

with the clinical history, we will note the following causes for gangrene in athero- and arteriosclerosis: first, that the circulatory inadequacy or insufficiency is partly due to the loss of elasticity in the vessels, partly to concentric diminution of the lumina of the vessels through atheroma, thickening of the intima, and calcification; second, that these stages are not sufficient to account for the sudden advent of gangrene in some cases, nor can other sources, such as cardiac weakness and trauma alone, be considered sufficient as immediate causes. But, there is a distinct pathological explanation in the occlusion produced by sudden thrombus formation. This usually occurs in the popliteal artery and extends upward into the femoral, more frequently passing downward into the posterior tibial artery. Histological examination of the femoral, popliteal and posterior tibial arteries in such cases, has demonstrated conclusively the importance of the rôle of thrombosis in the causation of the gangrene, the thrombus being discovered in various stages of organization, depending upon its age, that is, upon the time that has elapsed between the onset of its formation and the time of amputation of the limb.

Clinical History.—There is usually a previous history in elderly individuals (over forty-five years of age) of intermittent claudication or indefinite pains in the lower extremities, particularly in one limb. Suddenly, the patient will develop the following symptoms: trophic disturbances terminating in gangrene of small extent (one toe or more); or dry gangrene of a toe or toes, the foot, or portion of a leg; or, extensive dry or moist gangrene. In other cases the signs of sudden impairment of circulation due to thrombosis of the popliteal or femoral arteries make themselves manifest without the development of ulcer or gangrene. These are sudden pain in the calf of the leg or foot, attended with paresthesiæ, coldness, pallor and weakness of the limb. Examination reveals absence of pulsation in the dorsalis pedis, posterior tibial, possibly also in the popliteal arteries, pallor of the foot, slight erythromelia on depression of the limb, at times thrombosed veins, particularly the external saphenous. Hemorrhagic areas and cyanotic patches suggestive of impending gangrene may also appear. Improvement in circulation may then take place, so that the limb gradually becomes warm, the pallor and cyanosis disappear, a state of chronic erythromelia (rubor) being usually the manifestation of improved circulatory conditions. Sooner or later, however, even such cases may have fresh attacks of thrombosis leading to gangrene.

A study of the vessels in such cases has shown either recent organizing thrombi in the popliteal artery, or, a combination of these clots with old organized clots, the recent thrombosis extending for a variable distance downward into the posterior tibial artery. From the observations on the conditions of the arteries, it seems that extensive obturation due to atherosclerosis, atheroma, etc., and old thrombosis in the popliteal artery may be compatible with fairly good circulation of the limb. *But, when an additional extensive recent thrombosis takes place, or, when extraneous causes (cold, cardiac weakness, etc.) are added, the limb succumbs to the mortifying process.*

Whilst certain patients offer a history that suggests clearly the occurrence of a fresh accession of thrombus formation, there are others in whom there is merely the story of a trophic lesion apparently precipitated by cutting a nail with injury to the nail-bed or surrounding skin, or by an operation for ingrowing nail. When an ulcer thus formed is suddenly complicated by a turn for the worse, with more deficiency of local circulation, it is usually due to recent thromboses in the popliteal or posterior tibial arteries.

After pain in a toe (usually the big toe) for a variable time, a period of intermittent claudication, a trauma, or without cause, an ulcer forms and

refuses to heal. There is gradually deepening cyanosis and coldness about the affected region. Erythromelia, and ischemia can be elicited and the pulses up to the femoral are usually absent. Suddenly the toe begins to look black and the foot becomes colder, gangrene being imminent (recent thrombosis?). Even such cases may respond and heal under the postural method.¹

Bland thromboses are apt to occur in the popliteal or upper posterior tibial artery with extensive gangrene of sudden advent as a sequence. The lesions of thrombo-angiitis obliterans, too, may have preceded with participation of some of the peripheral vessels, such as the dorsalis pedis and plantars. When alterations in the latter are of very long standing and secondary degenerative changes (calcification) coexist, a clinical differentiation from arteriosclerosis may be no longer possible. The cases allow of the following grouping:

(1) Advanced atherosclerotic diffuse processes, thrombotic occlusion and organization in the peripheral vessels with superadded recent bland thrombosis leading to gangrene of sudden onset.

(2) Advanced atherosclerotic diffuse processes, old thrombo-angiitis obliterans of limited extent in the peripheral vessels, recent bland thrombosis and gangrene.

An excellent example with thrombosis of the popliteal artery is the following:

S. S., male, age 59 years, had intermittent claudication and cramp-like pain in the right leg on walking, dating back 4 months. Six days before he reported for examination, an ulcer appeared over the right big toe, which increased gradually in size without much pain. Two days thereafter the toe became black, and the patient suffered repeated chills. He had noticed redness, tenderness and swelling of the right leg the following day. He had no other symptoms.

Physical examination (author's notes taken January 30, 1915) showed the big toe of the right foot to be bluish and livid, and evidently the seat of rather extensive gangrene, the cyanotic color being rather deep, the toe cold. At its root the skin was very deep blue, blackish and in the early stages of gangrene. The color was apparently altered by reason of the detachment of the epidermis and a collection of fluid (serum and blood) underneath it; in short, a large blackish bleb of irregular contour. A bulla was also noted over the second toe which was almost completely black. The third toe was also cyanotic. The fourth toe showed several black blebs, and the fifth toe a very large bleb of similar nature. The dorsum of the foot showed the changes above described over the toes, the greater part being reddish because of an inflammatory process. The usual evidences of rapidly spreading moist gangrene of the foot developed. Running upward along the internal saphenous vein and well into the saphenous opening, there was a strand of lymphangitis.

On elevation of the foot pallor ensued, particularly at the roots of the toes where this was very marked in contrast to the very bluish discoloration of the gangrene. The dorsalis pedis, posterior tibial and popliteal pulses were absent, the femoral present.

A section of the limb amputated through the lower thigh, January 30, 1915, was examined January 31, 1915, and showed the following conditions, as recorded in the protocol:

The Gangrene.—The blackish bullae contain sanguinous fluid, reddish, some with dark blood, others with light, and some with serum and blood. On cutting the skin we find that the bluish discoloration penetrates for varying distances, 1 mm. or more. Along the course of the internal saphenous vein, there is evidently lymphatic infection, for pus can be squeezed out of the lymphatics.

The Vessels.—The popliteal artery at the site of amputation just above the knee in its lower fourth, contains fairly firm organized clots with marked atherosclerosis of the vessels, a sort of glassy or gelatinous clot such as we get in atherosclerosis with secondary thrombosis. As the artery is traced downward, *the clot becomes more red, finally terminating in a very recent red clot* just above the bifurcation of this vessel. It is apparent that there was an old thrombotic process followed by recent extension of the clot (tail portion). Below this, the posterior tibial artery simply shows the lesion of atherosclerosis, as does also the peroneal, but without thrombosis. In the lowermost parts of the posterior tibial artery are some closed areas that may either be due to an old thrombo-angiitis obliterans plus arteriosclerosis

¹ See Chap. LXV, p. 380.

and thrombosis, or simply arteriosclerosis plus thrombosis. The anterior tibial in its upper half is patent and shows the lesions of arteriosclerosis. The lowermost portion is closed here and there. Macroscopically differentiation is impossible between an arteriosclerosis plus thrombosis or thrombo-angiitis obliterans. From a clinical standpoint, the features of arteriosclerotic gangrene were here presented. The absence of an old history of thrombo-angiitis obliterans, the age of the patient, the rather short duration of the symptoms of intermittent claudication, the wet type of gangrene, the bullæ, the diffuse infection and lymphangitis, all these were rather suggestive of arteriosclerosis. However, an old thrombo-angiitis obliterans of limited extent in a latent or cured stage with superimposed arteriosclerosis and secondary thrombosis of the popliteal artery could have produced a similar outcome.

Such sudden gangrene and lymphangitis are usually encountered where *rather extensive thrombosis takes place in larger arteries*, a lesion superimposed upon an old occlusive process in other territories. Such vascular occlusion can be clinically interpreted in the light of two possibilities: (1) thrombo-angiitis obliterans with secondary degeneration or atherosclerosis followed by bland thrombosis in previously patent arteries; and (2) arterial disease of the arteriosclerotic type with here and there areas of bland thrombosis secondary to the arteriosclerotic process.

In several instances of the above type of clinical history and arterial lesions with gangrene, data could be obtained to warrant the following conclusions.

Conclusions.—(1) In some cases we seem to be dealing with arteriosclerotic changes, popliteal obturation through old thrombosis, with recent extension of the thrombus downward to the bifurcation of that vessel.

(2) Marked infection of recent advent follows, thrombotic gangrene of considerable areas, and extensive lymphangitis.

(3) In elderly people it is difficult even at autopsy of the limb to determine with certainty as to whether there exists one of the following: simple arteriosclerosis with thrombosis; or thrombo-angiitis obliterans in peripheral vessels upon which is engrafted a secondary arteriosclerosis and a subsequent recent accession of thrombosis.

Arteriosclerosis with Thrombosis of the Larger, More Central Paths.—It is most difficult to differentiate between embolic gangrene, particularly of the lower extremity, and thrombotic processes, when gangrene is of sudden advent and complicates intensive athero- and arteriosclerosis, especially in diabetes. We are called to see a patient usually over 40 years of age, who gives a history of having had a bad heart, some evidences of arteriosclerosis with or without diabetes. Suddenly there is pain in the calf of the leg, in the foot or the knee, the limb becomes powerless and cold, and gangrene rapidly sets in, the extremity below the knee, or even up to the upper fourth of the thigh showing the usual signs of imminent gangrene. None of the pulses below Poupart's ligament are detectable.

At amputation through the upper fourth or upper fifth of the thigh, the femoral artery and vein are found closed with recent red blood clots, and there is very little or no bleeding. But the artery shows intensive atherosclerosis and its lumen is reduced to less than half of the normal.

So, also, is it hard to distinguish between an embolism of the external iliac or common iliac, and thrombotic occlusion superimposed upon intensive atherosclerosis, a lesion not infrequently seen in the popliteal artery. Wherever the condition of the heart warrants the diagnosis of cardiac thrombi, and whenever the future course of the malady demonstrates that emboli are being cast off from time to time into other territories, the embolic nature would seem to be established. In the absence, however, of such a course and such cardiac signs, we may be dealing with a thrombotic process superadded upon intensive atherosclerosis.

Although the more usual lesions leading to gangrene due to extensive occlusion and thrombosis in the peripheral territories are below the knee and at the popliteal, an acute advent of thrombosis or embolism in the external iliac or upper femoral arteries is occasionally seen. In these cases the gangrene is of sudden advent, extensive, and gives the picture of the embolic type described under embolic gangrene. The femoral artery may be found patent up to within one or two inches of its origin, where a tail clot of a femoral clot higher up is encountered. The following brief history will elucidate.

B. H., female, age 67, arteriosclerotic, gives a history of the sudden advent of coldness of the right foot and leg, 10 days ago, without abdominal pain or cardiac distress. Immediately thereupon all the signs of dry gangrene made their appearance.

Upon physical examination well advanced gangrene of the right foot is seen; cyanosis to the upper fourth. The thigh is warm to the lower third.

February 12, 1923, circular amputation through the upper fifth; very little bleeding although no tourniquet applied. The femoral artery does not pulsate, and on section a red clot, representing doubtlessly the tail clot of a primary clot higher up, was removed. The saphenous vein in the uppermost part is thrombosed. All the large veins are distended. The femoral artery is atherosclerotic, dilated, and eroded.

Conclusions.—The primary clot, therefore, must have been situated above the point of ablation somewhere in the external iliac or most proximal part of the femoral artery.

Atrophy as a Sequel.—*Pseudophthisis* of the foot and leg or *atrophy* (of vascular origin) is a chronic condition not infrequently the outcome of thrombosis of the popliteal or of the other peripheral vessels, superimposed upon nutritive disturbances already the result of arteriosclerotic vascular disease.

In a patient with evidences of diseased arteries, either objectively demonstrable or subjectively manifested by such symptoms as intermittent claudication, the following sequence of events may occur 1st, an attack of thrombosis; 2nd, abatement of the acute symptoms with or without appearance of trophic disorders; 3rd, a condition of chronic withering or atrophy (for which the author suggests the name pseudophthisis or vascular atrophy) or, in lieu of this, gangrene; and 4th, eventually gangrene following the previous period after an interval of months or years. In rare instances the condition may develop insidiously *without any history of an acute attack of thrombosis*.

Clinical Course.—With numerous variations but to a certain extent conforming to the type exhibited by the case next cited this condition is traceable to an "attack of thrombosis" with the following symptoms: sudden pain in the calf or in the foot, inability to walk, with pallor of the forepart of the foot, coldness, marked blanching on elevation, the dorsalis pedis, posterior tibial and popliteal pulseless, while the vessels of the other leg are pulsating. The blanching of several of the toes may be very marked, and the superficial veins, such as the external saphenous, may be palpable and tender. After the commencement of these symptoms, areas of gangrene may rapidly develop, or trophic disorders which become more striking when the foot hangs down; but in the absence of these, pseudophthisis or vascular atrophy gradually ensues.

Acute attack of popliteal thrombosis in arteriosclerosis, subsidence of threatening gangrene, development of chronic atrophy of leg, semi-invalidism for two and one-half years eventuating in gangrene, amputation, recovery.

S. K., male, aged 65 years, a diabetic thought he was attacked with "lumbago" 5 days previously, though the chief complaint was "cramps" in both legs, particularly in the right. Early this morning (June 12, 1915) there was pain in his right leg, which seemed to get cold and numb, so that he could not bear his weight on it.

Physical Examination (Author's notes June 12, 1915).—The forepart of the right foot shows distinct pallor, with an increase in intensity and extent of the blanching, when the foot is elevated. There is moderate rubor in the pendent position gradually giving way to cyanosis; the foot is cold and the dorsalis pedis, posterior tibial, and popliteal arteries *do not* pulsate whilst they are easily palpable in the other extremity.

A hard cord occupies the lower three fourths of the course of the external saphenous vein.

Diagnosis.—Thrombosis of the popliteal (possibly posterior tibial) artery with threatening gangrene and thrombosis of the external saphenous vein in an arteriosclerotic.

First Stage.—June 14. The color of the toes is slightly improved. When the foot is exposed for a short time, it becomes slightly cyanotic. In the pendent position there is a combination of cyanosis and rubor, and the patient complains of heaviness and pain in the sole. The outer border of the foot is red—this region described by the patient as having a “hot poker” applied to it. The thrombophlebitis of the external saphenous vein seems to have extended upward slightly. Over the mid-dorsum of the foot there is a patch of redness enclosing punctate ecchymoses (foreboding of trophic lesions). These hazy lesions are intensified and easily discernible when the foot hangs down. On the following day the red area was more distinct and the hemorrhagic spots were converted into dark minute scabs.

Treatment.—Warmth, rest and Allen method for the diabetes instituted immediately; postural procedure on the 20th of June.

Second Stage of Subsidence with Impending Trophic Lesions.—June 24. Area on dorsum of foot in about the same condition; rubor in pendent position more marked. Pain in the limb has disappeared.

July 1. Distinct improvement, color better, almost normal except for the rubor.

July 25. The color of the foot is good except that the right foot is much redder than the left, and suggests the appearance of the leg in thrombo-angiitis obliterans when in the state of chronic erythromelia (chronic erythromelia in arteriosclerosis).

August 1. Now able to bear weight on right foot for a few seconds; blanching still marked on elevation, general color of foot good.

From now a gradual improvement without development of gangrene or ulcers, the extremity passing from the second stage of abatement into the beginning of the third stage of chronic vascular atrophy.

From August, 1915, to December, 1916, he has been an invalid, unable to walk, although now (December 1, 1916) he is able to get about with a cane.

Condition of Right Leg.—December 1, 1916. There is marked atrophy of the foot and leg, chronic rubor even in the horizontal position, this extending to one third way up the leg. Ischemia is demonstrable upon elevation through an angle of 30° , and intensified reactionary rubor shown after preliminary elevation through an arc of 30° to 45° . The left leg shows very slight rubor and ischemia on elevation—evidences of arteriosclerotic occlusion of vessels. (Third stage of atrophy now marked.)

March 28, 1917. Author's notes read: For 23 months the right leg has been in a stage of chronic (vascular) atrophy, with constant tenderness of forepart of foot, dorsal and plantar regions, with chronic rubor and with outcropping of evanescent ecchymoses.

April 26, 1917. Right foot.—Very much withered, hemorrhages numerous, some conglomerate in thickly aggregated areas, some confluent in small patches, others discreet over the dorsum. The toes are tender and cannot be separated without causing pain, although there are no fissures. Subjectively, the foot feels cold, ankles and dorsum painful, and feels as if some “iron weight” were applied.

Besides the erythromelia, there is noted a clonus or intention tremor of the foot as soon as it is flexed and not steadied against some object.

November, 1917. Gradual onset of dry gangrene with involvement of the toes gradually (December, 1917) extending upward (fourth stage of gangrene).

December 31, 1917. Amputation by the author just above the lower third with excellent result.

Pathological Examination.—The vessels showed the usual picture of marked arteriosclerosis with *thrombosis of the popliteal and upper arteries*.

Summary of the Issue after Thrombosis.—There may be frequent attacks of thrombosis over various territories with the following sequences:

(1) When sufficiently extensive, thrombosis may lead to immediate gangrene.

(2) It may cause merely trophic disturbances.

(3) It may give rise to the clinical picture of an “attack of thrombosis.”

(4) It may lead to mere atrophy (chronic vascular atrophy), or pseudo-phthisis of the limb; or,

(5) To a slight aggravation of the existing symptoms, of which intermittent claudication is the most striking; or to exacerbations of pain and tenderness, localized and roughly in the course of some larger deep vessels of the leg. A reference to similar phenomena and to spontaneous paroxysms of pain has been made in the Chapter on Pain in Thrombo-angiitis Obliterans.

CHAPTER LXX

ARTERIOSCLEROTIC GANGRENE WITH DIABETES

This should not properly be classed as a distinct form of gangrene (so-called diabetic gangrene), inasmuch as the pathology is the same as that of arteriosclerotic gangrene. The mortifying process should not be regarded as being due to the diabetes, but primarily as the result of extensive arterial obliteration. The disease may take a course somewhat different from simple arteriosclerosis because of the presence of the complicating diabetes. The symptomatology may be identical with that discussed under arteriosclerotic gangrene, or may be modified after trophic disorders and gangrene have definitely developed by reason of the hyperglycemia.

When ulcers are present, a phlegmonous process is more apt to ensue with the trophic disorders as the starting point. Necrosis of the deeper tissues is likely to be more extensive, and moist gangrene is more frequently seen. As far as the changes in the arteries are concerned, these are identical with those of arteriosclerotic gangrene, and the calcification and atheroma are usually intense.

Cases of diabetes in elderly people with fairly marked arteriosclerosis may present none or very few of the typical signs of impaired circulation, and still may develop patches of gangrene. Such gangrene usually eventuates after traumatism, thermal or mechanical. The development of a gangrenous patch over the shin bone after an abrasion, or after careless rubbing, scratching or massage is common. The abrasion, scratch or burn becomes converted into a small area of dry gangrene, involving merely the skin, rarely the subcutaneous areolar tissues.

On examination it will be found that blanching on elevation is absent. Erythromelia or reactionary erythromelia are also absent. The dorsalis pedis and popliteal may pulsate. The general color of the limb is good. In short, there are none of the usual manifestations of circulatory deficiency, and yet gangrene occurs.

These are the cases in which inadequacy of circulation is not sufficiently great to produce definite objective phenomena of vascular obturation in the peripheral parts. And still the narrowing and rigidity of the arteries, coupled with the presence of the metabolic deficiencies due to the diabetes, are sufficient to lead to gangrene of the tissues upon the mere action of a trifling trauma. The prognosis in these cases is usually good if treatment be directed toward the diabetes, if infection be prevented by giving free exit to pus, when it collects under the gangrenous patches of the skin and if the author's "Postural Method of Treatment" be employed together with other methods for enhancing the circulation.

Pathology.—We have grouped both the arteriosclerotic and diabetic cases together, for the pathology of the vessels is the same. A study of the con-

dition of the arteries and veins in limbs amputated for so-called diabetic gangrene, reveals the fact that in each and every instance we are dealing not with a gangrenous process due to the diabetes *per se*, but a mortifying process dependent upon extensive arterial disease.

In both arteriosclerotic and diabetic cases there is an extensive and intense athero- or arteriosclerotic process. In some cases there is *marked occlusion* due to the heaping up of atheromatous and calcific material or to a combination of this process and secondary thrombosis, or a moderate degree of atherosclerosis with obturating thrombosis. These cases may be grouped under the caption—*intense, obturating atherosclerotic process*. In another series of cases we find that, although very few of the vessels are completely closed, the atherosclerotic process is very extensive and intense making the vascular walls rigid, or producing a dilatation or pouching of the walls of many vessels. Both of these lesions will have as their sequence impaired nutrition of the parts, by virtue of the loss of elasticity in the arterial walls. This type may be grouped under the caption—*athero-sclerosis with slight or no occlusion*.

Common to both types, the diabetic and arteriosclerotic, is the fact that the larger veins are but moderately involved, although they may have suffered a moderate degree of endarteritis or thickening of the intima.

The arterial lesions may be summed up as follows: extensive degeneration of the arterial walls, intense atherosclerosis, calcification, sometimes bone formation, often occlusion of a large part of a vessel's course, the arteries being converted into rigid pipe stems; at other times, less pronounced atherosclerosis with dilatation of the vessel walls in places, or a combination of intense atherosclerosis with thrombosis. Where the latter occurs, elastic tissue stains show proliferation and heaping up of the elastic layers or lamellae and that the remnant of the lumen may be occluded by organized clot. Another type of lesion is that in which marked calcification of the vessel walls takes place, sometimes attended with bone formation.

Complicating Infection.—The extensive phlegmonous inflammation so frequently seen in diabetic cases is usually associated with gangrene of at least the skin. Treatment is often delayed, and incisions made too late because the temperature may not be high at the onset, the pain only slight, and their external manifestations in no measure corresponding to the extent of the process in the depth. Whenever we meet with a small focus of infection in a diabetic, palpation for tenderness over the focus of the infection usually near the base or over one of the toes, is in order. Invasion of the plantar tissues and dorsum rapidly takes place, so that careful watch must be made from day to day for the development of tenderness along the plantar aspect of the foot as well as over the dorsum. In this way only can evidence of infection be elicited long before suggestive or external manifestations appear. As a rule, a consultant is called to see such cases when the phlegmonous process has already made considerable progress in the deeper parts although the surface changes may be but slight.

Given a small focus of infection between the web of the toes, near the base of the toe or elsewhere in this region, a sloughing wound is apt to develop. Subsequent to this, tenderness may be elicited along the plantar aspect in a line leading from the point of original infection, or along the dorsum. Infection develops, a red area over the dorsum can be made out, and discoloration into a bluish or purplish hue is often seen. There may be but very little infection under the skin; but slight as this may be, it may suffice in these cases to compromise the circulation of the superimposed integuments, and lead to gangrene.

But even with the development of such very evident signs of infection—redness, tenderness and fever—a clinician is apt to underestimate the extent of the process both under the surrounding apparently healthy skin, and into the depth.

When incision is made into such areas the skin will frequently be found to be undermined for a considerable distance by a sloughing suppurative process, and the deeper tissues too. The tendons, fascia, and muscles will be seen to have undergone a similar destruction even though this be unsuspected.

Diabetic Cases.—The following abstract from the author's notes on the pathology of the vessels in amputated legs of cases of so-called diabetic gangrene will illustrate in detail the type of lesions that are found.

I. *Extensive Atheromatous and Calcific Obturation.*

P. A., April 1, 1909 (diabetic gangrene): Right leg ablated at the knee joint; one ulcer situated at the outer border of the foot, corresponding to the head of the fifth metatarsal; it is about the size of a dime, covered with sluggish, necrotic granulations; a secondary ulcer, slightly larger, more superficial, found at the head of the first metatarsal, at the inner border of the foot.

Popliteal artery is atheromatous at the point of ablation, possibly thickened but not occluded.

Posterior tibial is almost completely closed by atheromatous plaques. Its middle third is almost completely closed by degenerate atheromatous masses; the lower third shows similar lesions.

External plantar is almost completely closed by atheroma.

Peroneal in its upper part is almost completely closed by a series of atheromatous plaques; throughout the remainder of its course, there are yellowish, rounded atheromatous plaques and diffuse atheroma.

Anterior tibial is practically closed by the atheromatous process and calcification throughout its entire extent.

Dorsalis pedis is open; but markedly atheromatous. The veins are all open; the external and internal saphenous are normal.

There is no periarteritis.

Summary.—Ulceration and beginning gangrene in a diabetic; extensive atherosclerosis with occlusion of many of the arteries, the veins being open. A typical example of the occlusive variety of *the atherosclerotic process*.

II. *Atherosclerosis with Thrombosis.*—As an example of somewhat less marked atherosclerosis, associated, however, with obliterative thrombosis, we have the following case:

R. A., aged 62 years, "diabetic gangrene." Right leg: ablation $6\frac{1}{2}$ inches above knee joint. The dorsum of the big toe and adjacent surface of first metatarsal bone are the seat of beginning gangrene that has extended almost to the head of the metatarsal bone. This area is covered with a brownish green discolored skin beneath which lies a pool of fluid; when this necrotic material is wiped away, the tendon sheath of extensor muscles of toe and underlying bone are exposed. The necrotic material has insinuated itself beneath and around the extensor tendons of the second and third toes, downward as far as the base of these toes, and upward as far as the head of corresponding metatarsal bones. The epidermis covering the sole is easily stripped off over the anterior three-quarters of the foot, exposing an irregularly quadrilateral gangrenous patch about the center of the foot. The appearance of this patch is like that described as occurring on the dorsum. It extends upward between the plantar fascia and muscle groups, apparently coming into contact with the first and second metatarsal bones and communicating with the gangrenous area on the dorsum.

Femoral artery is sclerotic and brittle and, at one point near the lower end, there is a large ulceration of the intima about 3×7 mm. Just below this there is another ulceration with some undermining of the intima by extravasation of blood. The vessel itself is patent. The femoral vein is only slightly thickened and is patent.

Popliteal artery is patent throughout. Its wall is much thickened and somewhat calcareous, especially in the upper part, where there is an encircling band of calcareous material about 2 mm. in breadth. The intima is smooth, but there is diffuse atheroma, this being especially marked about the orifices of smaller branches. The accompanying vein is only slightly thickened and is open throughout.

Posterior tibial, at its origin, and for a distance of about 11 cm. is patent; from this point on, there is an obliterating thrombosis of the vessel. The occluded portion is contracted. The vessel, as a whole, presents only a moderate degree of sclerosis, this being more marked from the point of thrombosis down.

Peroneal artery, at its origin, and for a distance of about 4 cm., presents a similar picture to the posterior tibial. In the rest of its course there is complete obliteration by an old, white, organized thrombus. The accompanying veins do not show as much thickening as posterior tibial, and are patent.

Internal saphenous vein shows marked thickening of wall, so that the vessel can be rolled beneath the finger like a cord; it is, however, open throughout.

Anterior tibial shows a process similar to that involving the femoral though less extensive. Toward the lower end there is considerable narrowing of the vessel as a whole, but the lumen is unimpaired.

Summary.—Gangrene associated with arteriosclerosis and atheroma of the femoral vessel; extensive obliterative thrombosis and atheroma of the posterior tibial and peroneal arteries with thickening of the internal saphenous vein.

Another instance of extensive arterial disease is seen in the following case.

III. *Extensive Atheroma, Thrombosis with Puriform Necrosis.*—Many valuable clinical and pathological data are afforded by the following case of bilateral diabetic gangrene.

It will illustrate:

1st. That the antecedent history may evidence months or years of trouble in both limbs, first as localized trophic disorders and gangrene of very limited extent, involving merely superficial tissues or a whole toe, but finally more than two years later (in the case to be cited) eventuating in gangrene of first one, then the other lower extremity.

2nd. That characteristic in the diabetic cases is the insidious destruction, disintegration and infection of the deeper tissues, muscles, tendons and, even bone, masked by the superficial parts to such a degree, that often only considerable experience and very careful observation will succeed in giving the observer a proper estimate of the degree of necrosis present.

H. B. (May 10, 1905) male, age 52 years, diabetic for thirteen years, had the third toe of the right foot removed for gangrene. Two years previously a patch over dorsum of left foot had become gangrenous, was removed and healing took place again. In April, 1905, a gangrenous area developed on the sole of the left; this separated spontaneously and healed.

In May, 1907, the left leg was amputated through the thigh because of extensive gangrene, with recovery.

In June, 1907, a small ulceration appeared on sole of right foot, which became dusky red in color. Since then the gangrene has spread.

Local Physical.—There is a gangrenous area extending over almost entire dorsum of right foot from the toes to the ankle. The toes are reddened but not cyanosed. The skin over plantar aspect of the sole also gangrenous. The parts are very tender, feel hot and show inflammatory changes.

July 30. Area of gangrene on dorsum of foot has extended in lateral directions. From the ankle upward to about the middle of the leg there is decreasing induration and redness. The sensitiveness of the part is more marked as one proceeds upward. The sole of the foot is swollen, cold, and in its greatest extent not painful.

Operation July 31, 1902. Amputation above knee (right).

August 3rd. In one hour this A. M. patient passed into comatose condition, and in spite of reactionary measures died.

Gross Pathology of Extremity.—Right leg ablated five and a half inches above the knee joint. Middle toe removed at previous operation, same cause. Extending from inner margin of the sole of the foot and occupying the middle two-thirds of the inner surface across the dorsum and three-fourths of the outer surface of the foot, is an irregular area of gangrene covered with a black slough. The slough is very friable, easily removed, exposing the underlying necrotic tendons and intervening tissue; in places the bone is exposed. The adjacent skin is undermined by *purulent necrotic material*. The region of the ankle is edematous and the epidermis comes away in big patches. The lower half of the leg no longer shows the redness observed clinically.

Extending upward from the outer side of the ankle beneath the tendon of Achilles and along the outer part of the posterior surface of the leg there is purulent or necrotic material extending half way up the leg between the tendon Achilles and the deep plane of muscle. This purulent material is also found beneath and between the muscle and tendons of the deep plane, the muscles themselves showing some gangrene. On the inner side of the tibia between the bone and the overlying skin and on the outer surface of the leg between muscle and the skin there is a large area of sloughing material which does not involve underlying muscle but chiefly the subcutaneous tissue, extending upward half way to the knee.

Femoral vessels show periarteritis. Both vessels patent. Femoral artery wall is thickened, in places calcareous, and in some places thicker than in others. The intima shows small patches of atheroma, especially marked transversely. The intima and sub-endothelial layers are thrown into many transverse ridges springing from a median, longitudinal ridge. Between the transverse ridges are well marked pockets or depressions. The vein shows considerable thickening of the wall.

Popliteal vessels patent. The process as noted above in the femoral, namely the periarteritis, thickening of the vessel wall, atheroma, transverse ridges and calcareous patches are even more marked here. The transverse ridges require further comment as in several places they have elevated the intima into a *constricting ring* which has markedly decreased or stenosed the lumen at these points. The vessel above and below such a ring or stricture forms a somewhat dilated pouch. At the lower end of the popliteal joint above the bifurcation, there is a well marked plaque formation of the entire vessel wall (bone?). The vein shows thickening of the wall more markedly in some places than in others.

The *posterior tibial* just below its bifurcation downward to its termination is completely occluded by an old organized thrombus. The vessel itself is very much smaller in caliber than normal, *calcareous*, and shows large amounts of periarteritis. The *venæ comites* are thickened.

The *peroneal artery* shows continuation of process noted above in the popliteal and femoral, not quite so marked as in the popliteal. The peroneal vein is somewhat thickened.

The *anterior tibial artery* is like the posterior tibial artery of very much smaller caliber than normal and completely occluded by an old, white thrombus. The accompanying veins have thickened walls.

The *dorsalis pedis artery*, as far as it can be traced shows a continuation of the process noted in the anterior and posterior tibial.

The vessels below the ankle could not be worked out on account of necrosis.

CHAPTER LXXI

ARTERIOSCLEROSIS—DIAGNOSIS

Arteriosclerotic Cases Mimicking or Simulating Thrombo-Angiitis Obliterans.—When we are dealing with elderly individuals over 50 years of age, who show evidences of the existence of a generalized atherosclerosis or arteriosclerosis of the vessels of the extremities, the differential diagnosis from thrombo-angiitis obliterans may be difficult. The cases observed by the author have been numerous, but a mere indication of some of the types can be mentioned here. The histological pictures have proven beyond peradventure (Fig. 124) that the two processes may coexist.

Type I.—Thus, there may be a history of intermittent claudication for many years (S. P., 65 years of age) with coldness of the extremities, even with attacks of thrombosis of the veins of one or both legs, with the development of ulcers and pain in the toes and foot. On examination, all of the vessels of both extremities may be found apparently closed. There is marked chronic erythromelia, marked reactionary rubor, ischemia and cyanosis. Pathological examination of the vessels in such cases will show the lesions of arteriosclerosis with the superimposition of secondary thrombi that are *not* of the thrombo-angiitis type. (Arteriosclerosis plus attacks of thrombosis.)

Type II.—Most of the cases who have had symptoms for long periods failed to seek our advice before the advent of gangrene or trophic disturbances, frequently consulting the orthopedist or medical man who may be inclined to overlook the true nature of the trouble, diagnosing flat-foot. They have pain in the calf of the leg, ankle or foot, particularly on walking for a long time. On examination, one or both feet appear to be blanched, this blanching extending for a variable distance over the dorsum of the foot or a little farther up, depending upon the extent of the involvement, or it may simply affect the toes. With this, there are erythromelia, particularly



FIG. 146.—Calcification of posterior tibial artery in arteriosclerosis.

in the pendent position with or without cyanosis, absence of the dorsalis pedis, posterior tibial, and popliteal pulsations. The reactionary rubor comes on in the form of red patches. Associated are other evidences of arteriosclerosis.

Such cases are difficult to distinguish from thrombo-angiitis obliterans or from associated thrombo-angiitis and arteriosclerosis.

Roentgen ray examination is of great aid, firstly in the detection of calcified arteriosclerotic arteries (Fig. 146), and secondly, in estimating the amount of bony destruction present. In the arteriosclerotic affections of the vessels of the lower extremities, notably when attended with diabetes, the extent of the necrosis of bone is apt to be minimized by the clinician

when a mere sinus or small area of superficial gangrene is present. For, the disintegration not infrequently is more rapid and far reaching in the soft tissues, tendons and bone, than in the visible parts. It is the insidious progress of an indolent type of infection coupled with the deep necrosis that gives pictures such as are exemplified by Fig. 147 at a time when the



FIG. 147.—Insidious destruction of bone with necrosis and gangrene, associated with arteriosclerosis.

patient is still up and about, and quite unaware of the gravity of the situation. In such cases the Roentgen ray examination will demonstrate firstly, calcified arteries; secondly, atrophy of the bones of the foot, without the disappearance or blurring of the distal phalanges so characteristic of Raynaud's disease, and thirdly, destruction of bone. Such bone disintegration is not limited in extent as in Raynaud's disease, but may involve many phalanges, the metatarsal and even the tarsal bones.

L. G., male, 50 years of age (diabetic and arteriosclerotic) had had a sore fourth toe on the left side for some three months prior to October 6, 1915, this toe becoming gangrenous and separating. A sinus had persisted, attended with constant severe localized pain.

Physical examination shows a suppurating sinus, marked erythromelia, marked ischemia on elevation and absence of the dorsalis pedis and posterior tibial pulsations.

X-ray examination October 7, 1915, shows the dorsalis pedis and hallucis distinctly arteriosclerotic. The head of the fourth metatarsal and part of the shaft, as also about

one-sixth of its length at its distal portion, are completely destroyed. A faint indication of bone about the metatarsal phalangeal joint is still present. The shaft of the first phalanx of the third toe is very much thinned out, also being atrophic and involved. The distal part of the third metatarsal is also atrophic and disappearing, as well as the metatarso-phalangeal joint.

In short, destruction by necrosis of the head of the fourth metatarsal, atrophy and necrosis of the metatarsophalangeal (third), and marked atrophy of the first phalanges of the second and third toes.

Diagnosis.—Arteriosclerotic process with gangrene and trophic disorders with infection.

Except for the rare cases developing at a relatively early age (forty to fifty-five), the advanced age of the patient is significant. The history of intermittent claudication, the absence of arterial pulsation, evidences of defective local nutrition, the development of trophic disorders, the blanching of the foot on elevation with occasional rubor in the pendent position, the presence of distinct calcareous vessels in the Roentgen picture, and finally, the development of trophic disorders followed or attended by severe pain or gangrene, are the chief points to be relied upon for a diagnosis.

Although the chief clinical features of the disease, thrombo-angiitis obliterans, will be discussed later, the following differential points may be noted here. First, the symptoms in thrombo-angiitis obliterans, as far as the development of gangrene is concerned, are apt to come on much more slowly, the prodromal symptoms or signs lasting for weeks, many months or even years. Second, blanching and erythromelia (rubor) are not so regularly present in arteriosclerotic and diabetic cases, and if present, are usually not so marked. Third, gangrene may in either instance cover a small area at the beginning and slowly advance, but in arteriosclerosis and diabetic cases its advance is apt to be more rapid. Moist gangrene is less apt to occur in thrombo-angiitis obliterans. Fourth, alteration in the outward appearance of the limb in arteriosclerosis may be almost imperceptible before trophic disorders and gangrene develop, whereas in thrombo-angiitis obliterans the distinct evidences of the disease make their appearance many months previously. Fifth, the absence of migrating phlebitis, phlebotic nodosities, so typical of thrombo-angiitis obliterans is of differential value. Sixth, the occurrence of gangrene of the upper extremities is extremely rare in arteriosclerosis, relatively common in thrombo-angiitis obliterans. Seventh, racial (Hebrews), and sex (male) predilection so typical of thrombo-angiitis obliterans, does not obtain to a like degree in the arteriosclerotic forms.

CHAPTER LXXII

ARTERIOSCLEROSIS—PROGNOSIS

In arteriosclerotic gangrene the prognosis is usually grave. In general, the outlook is related to the age (the older the patient, the more dubious the chances) and the general systemic condition. When extensive thrombosis is absent, threatening gangrene may be controlled either spontaneously by rest, or, with the aid of the proper therapeutic measures. Or, the patient may get well with the mere loss of a phalanx or digit. Patients of very advanced age, with extremely poor circulation, must be regarded as gravely ill, for high amputation, above the knee or at the middle of the thigh, will

eventually become necessary. Even this procedure when it is well borne, may be followed by continued sloughing of the skin flaps, necrosis of the exposed tissues and finally a lethal outcome.

The outlook is always bad in cases of arteriosclerotic gangrene of the diabetic type. As a rule we are dealing with patients advanced in years. The arteriosclerotic process is intense. The vitality seems to be diminished, both by virtue of the condition of the vessels, as well as by the general systemic condition of the patient. In spite of the best conservative treatment, failure to heal even a small ulcer is common, and extensive, subacute, phlegmonous formation is to be expected in many of the cases. Even when a line of demarcation has developed, the spontaneous sequestration of the part and spontaneous healing is only to be regarded with a degree of hope in those cases where but a small part is involved, such as a toe or a part of a toe. When amputation above the knee has to be performed in diabetics, the danger of supervening coma is great.

This type of gangrene may be regarded as one of the least hopeful, the mortality being higher than in any other type of gangrene due to arterial disease.

Since the adoption of the insulin (iletin) method of treatment, the prognosis has become distinctly better, both in so far as the prevention of coma and a lethal outcome are concerned, as well as in enhancing the patient's ability to combat complicating infection. Perhaps with advances in the methods of administration of this substance, the outlook will be so much improved, that the gravity of impending coma will be greatly minimized.

Pessimism as to the likelihood of local healing after amputation of a toe or after the advent of infection, should not be carried so far as to reject all possibility of the success of conservative measures. Indeed, it will be pointed out in the chapter on Treatment that astounding results may be achieved even in the *diabetic cases* without sacrifice of the affected extremity.

CHAPTER LXXIII

ARTERIOSCLEROSIS—TREATMENT

The simple arteriosclerotic and diabetic cases may be considered together, although the special exigencies of the diabetic cases will require particular attention. Treatment includes the systemic therapy of the diabetes and generalized arteriosclerosis, and prophylactic treatment against complications. Local management comprises methods of enhancing circulation in the affected extremity, the care of trophic disorders, secondary local infection and methods of amputation.

Prophylactic Measures.—The patients with diabetes as well as those with uncomplicated athero- and arteriosclerosis should be given a list of rules that must be carefully observed, to minimize the chance of developing trophic disturbances and gangrene.

First, walking for great distances should be avoided, particularly if there is a history of intermittent claudication, cold extremities, previous attacks of gangrene, or trophic disorder, together with the objective findings by the physician pointing to impaired circulation, such as ischemia, pulseless vessels,

or erythromelia. Second, exposure to cold, with possible frost-bite is dangerous; even moderate degrees of cold are poorly borne. Third, the wearing of tight shoes should be carefully shunned. Wherever possible, a sojourn in a warm climate will be found beneficial. Fourth, all manipulations, such as cutting corns, callouses, ingrown toe-nails, bunions, should be left to a physician or surgeon, for, the very beginning of trouble is often traceable to the manipulations of a pedicure. Fifth, the smallest injury should be scrupulously cared for by a competent surgeon. Sixth, daily cleansing of the feet, with more than ordinary care, and the use of sterile dusting powder should be insisted upon. Seventh, tobacco and alcohol should be indulged in with great moderation, or not at all. Eighth, diabetes, if present, should be treated according to present day methods with a view to making the patient free of acetone and diacetic acid and reducing the sugar content of the blood.

Methods of Improving the Circulation.—These include, first, the author's postural treatment; second, the hot air treatment; third, the diathermic treatment; fourth, the heat of electric lamps; fifth, the thermophore.

All these methods may be given a trial. They are described under the section on thrombo-angiitis obliterans. They are not applicable, however, in all cases and only experience can teach us what the best methods may be in any given case.

The *postural treatment* (author's) which consists in the induction of a reactionary hyperemia in the affected part by preliminary elevation of the leg, followed by depression of the limb in a dependent position—may be used with some benefit in almost all cases, except where gangrene has already become extensive, where a phlegmon has developed, or where such changes of position are too painful to the patient. When recent extensive thrombosis has taken place, it is also contra-indicated.

The postural treatment, or exercises to induce rubor and an accelerated circulation must be varied in its method of application in each and every case. The period of elevation should be the minimum amount of time necessary to produce a frank blanching of the foot. This is usually about 30 seconds to 3 minutes depending upon the degree and extent of the vascular obstruction. The next period of depression (or of the hanging leg) is to be prolonged about 1 or 2 minutes beyond the time necessary for the induction of distinct rubor. An abridgement of this is then warranted, when the patient complains of increased pain in this position, or if the pain becomes unbearable after a given duration of time. The third position of rest in the horizontal may be extended at will beyond 3 minutes provided that this does not suffice to give enough repose to the patient. In general it should be longer in the atherosclerotic cases than in the younger people affected with thrombo-angiitis, since the former may find the treatment onerous unless sufficient intervals of rest are provided.

The *position of the resting limb* in all forms of obstructive arterial disease is a matter that has, as far as the author knows, received no attention on the part of the clinician. If careful observations on the appearance of such limbs in varying postures be made, especially after the induction and abatement of reactive circulatory manifestations, it will be noted that the color of the foot varies considerably when in the horizontal plane. Whilst a normal or slightly diminished flesh color is not infrequently seen even in advanced arterial disease, the affected foot will often evidence varying degrees of pallor. This may affect but one or more toes, or the forepart of the foot, or it may involve even some of the distal portions of the leg. Or, the dorsum or plantar aspect of the foot may show patches of blanching alternating with

pinkish or slightly cyanotic areas. All of these color manifestations must be interpreted as attesting a circulatory insufficiency in this position. And as such, we may deduce lessons of prophylactic and therapeutic value—to wit, that such limbs are not to be allowed to stay during their period of rest, in the horizontal position, but *somewhat depressed*; and just enough to bring about color evidences of circulatory activity. And so after testing the angle necessary to bring about the return of almost normal color, the patient must be instructed that this particular position is to serve as his horizontal. Indeed, it is well even when asleep to arrange the bed so as to conserve the angle previously arrived at. For, harmful as is the continued stasis induced by prolonged standing or walking, so also is one of continued ischemia, even if but slight. A position of elevation universally regarded as harmless must be avoided because of its depleting effect.

The Duration of the Postural Treatment.—If the series of elevation, depression and rest constitute a cycle, a repetition of these in the indicated succession would comprise a séance. The determination of duration and number of séances daily must necessarily depend on the condition of the given case, and on the experience of the physician. In the atherosclerotic cases, we must restrict the length and number of séances somewhat. A good rule to follow is to alternate séances of about 1 hour with the application of some form of heat for one-half to three-quarters of an hour, allowing hourly periods of rest for meals and continuing the treatment well into the evening. If this be too onerous, time may be given for an afternoon nap of 1 or 2 hours. The most reliable immediate measure of the efficacy of the method is the change in color in the leg, the appearance of trophic disorders, and the subjective state of the patient. All these should govern the treatment qualitatively.

Hot air treatment must be very carefully applied, and should exclude the part affected by trophic disturbances or gangrene. The temperature should be gradually elevated, being no higher than 125° to 150° F. at the beginning of treatment, and raised no higher than 220°. Séances of 15 to 45 minutes, 3 to 6 times a day have given good results. Great care must be exercised in the use of hot air to avoid burning the patient, since dire results may follow such additional insult to the already damaged part. Here too, in the presence of extensive gangrene, phlegmon formation, attacks of acute or recent thrombosis with threatened dry gangrene of a large portion of a limb, this method is contra-indicated.

The application of heat by means of special lamps will find use where a hot air apparatus is not obtainable. So also an electric thermophore is a valuable aid to other methods of treatment, and should be wrapped around the thigh and leg over a flannel bandage, the temperature being controlled by a thermometer.

The greatest care must be exercised in the use of hot air in the so-called baking apparatus or oven, both to avoid aggravation of the condition, and especially to escape the danger of producing burns. Any appliance of this sort should be set up and watched by a competent and conscientious nurse or attendant, lest the exposed and badly nourished skin come into contact with hot metal or with a lamp, with consequent jeopardy to the integrity of both skin and limb.

Since we have employed the postural treatment, it has been found advisable to alternate the séances with periods of hot air application, so that the number of each will vary. Where the exercises are well borne for an hour at a time, they may be followed by similar or slightly shorter periods of hot

air. We no longer believe that the reactionary circulation induced by heat is sufficiently intensive or lasting to be of appreciable service when one or two short applications are given daily. Our aim should be to enhance the circulation over greater parts of the *day and evening*, an issue obtainable only through intensive, repeated and prolonged methods. And so, our present rule is to give at least 4 or 5 hot air treatments or approximately as many as the postural exercises and the bathing periods (in the cases of trophic ulcer and limited gangrene) as the case will allow.

The diathermic treatment may be tried in the arteriosclerotic and diabetic cases, if thrombophlebitis, extensive gangrene, phlegmon, ulcer, and infection are not present. It is, therefore, limited in its usefulness to those early cases in which symptoms of intermittent claudication are present together with threatened trophic disorders and gangrene, without actual gangrene or ulceration.

Treatment of Trophic Disorders and Gangrene.—This includes (1) all those conservative measures which have for their purpose the attempts to heal trophic disorders, such as ulcer, infections and gangrene of small extent; and (2) methods of amputation.

Wherever possible, particularly in cases of arteriosclerotic gangrene, complicated with diabetes, every effort should be made to prevent extension of the local process, and to bring about a cure without amputation. Absolute rest and strict asepsis are essential. Where dry gangrene is present, diligent attention to cleanliness of the part, sponging with weak alcohol, powdering with dermatol or bismuth subnitrate, are measures that are indicated until sequestration or demarcation begins. Where sloughs are present, no attempts should be made to separate these artificially unless this can be done without causing too much injury. Where infection is present, daily baths of warm saline solution from 15 to 20 minutes, 2 to 6 times daily, followed by sponging with weak alcohol over the intact skin, and then the application of wet dressings (liquor Burrowi 1 part, glycerin 2 parts, water 3 parts, or 2 per cent boric acid) changed often, and kept moist without the use of impervious rubber tissue or other means, will tend to accelerate the separation of sloughs and limit the inflammatory process. Incisions must be made whenever there is an extension of the phlegmonous process, nitrous oxide gas, or nitrous oxide with oxygen being administered for this purpose. Local anesthesia should not be used under any circumstances. When a toe or a small part has become sufficiently loosened, the part may be removed under nitrous oxide gas. Or, when the gangrene is limited to one toe, or more, and the pain becomes too great to bear, the removal of one or more toes under nitrous oxide gas is indicated.

Treatment According to Case Types.—Although no rigid rules can be laid down for the indication and manner of application of the various methods, each and every case warranting special modifications, a general survey may be given that will clarify the principles to be followed. Here as well as with all forms of therapy, the treatment depends on the clinical form, stage and intensity of the lesions.

Let us divide the cases into

(1) Those with intermittent claudication, or occasional pain, or coldness, without trophic disorders or gangrene.

(2) Cases with evidences of arterial closure, that develop a minimal infectious lesion or trophic ulcer.

(3) Cases with chronic ulcerative or perforative (perforating ulcer), lesions *without* progressive and profound infection (phlegmon).

(4) Cases with any of the above and superadded attacks of thrombosis.
(5) Cases with atrophy or chronic withering of the extremity with or without intense chronic rubor.

(6) Cases with frank gangrene.

(7) Cases with any of the above complicated by (a) indolent, or (b) severe infection (with lymphangitis and possibly general symptoms).

(8) Cases with associated vasoneurotic crises may warrant trial of the Leriche operation (Chap. CV); these are described on pp. 578 et seq.

1. Patients who come to us with the story of difficulty on walking, vague pains or coldness of the feet, will rarely submit to a rigid regime even though apparently insignificant symptoms may be of grave import. As soon as the diagnosis of chronic impairment and deficiency of the circulation is made, the general advice both as to the prophylaxis and active therapy should conform in its rigidity with the gravity of the situation. And not only should we take the extent of arterial occlusion—as evidenced by the absence of pulses—into consideration, but importance should also be attached to the significance of ischemia, rubor, and the angle of circulatory sufficiency.

Where there is but very little pallor on elevation, little or no chronic rubor and the complaint of intermittent claudication is not marked, the importance of prophylaxis both general and local should be emphasized, and the evils that may ensue upon injudicious mode of living and excessive exercise should be brought to the patient's notice. The postural treatment should be begun so as to occupy at least 3 hours of the day and at least 1 (or 2) treatments with some form of thermic apparatus is to be suggested. The internal administration of iodides intravenously is lauded by some; and if there is any possibility of a luetic infection, antisyphilitic treatment is in order. For the well to do, a sojourn in a southern, warm climate during the winter months—during which time golf, sports, walking, tennis, etc. are to be interdicted—constitutes important prophylaxis. Massage is inadvisable, since the advent or onset of thromboses can never be foretold. Periods of rest after meals, with removal of all foot covering other than loosely fitting slippers and socks, avoidance of personal cutting of nails and corns, scratching, etc., are points not too negligible to be forgotten.

The question of "How long may I stand on my feet?" or "How far may I walk?" is aptly put by the patient and deserves careful consideration and deliberation on the part of the physician, whose answer should be founded on a careful clinical study of each case. Where we suspect possibly thrombosis of deeper arteries, or where the pain is sudden and intensive so as to awaken the suspicion thereof, the patient should be put to bed at once for periods of 1 to 3 weeks or more. Even thrombosis or thrombophlebitis of superficial veins—external or internal saphenous—may necessitate similar measures, and, in such cases the manifestations due to disease in the superficial and deep vascular channels should be carefully balanced and appraised.

Here, too, as in all cases, the circulatory sufficiency in the horizontal position is to be estimated, so that correct advice as to posture when sleeping, can be given. Whenever ischemia is present in the horizontal or very slightly elevated position, indicating that the encroachment of the disease is already of considerable extent, a moderate degree of downward obliquity of the limb (as previously ascertained) may be preferable.

2. *Cases with Arterial Closure that Develop Minimal Infections or Trophic Lesions.*—With the principles laid down in the preceding discussion well in mind as applicable in a general way to all cases, variations depend on the complicating manifestations, degree of vascular inadequacy and infection.

Whenever a small, apparently insignificant cutaneous lesion appears in cases of disturbed circulation of the extremities (particularly if of organic vascular nature) its importance must not be minimized and corresponding prophylactic and therapeutic measures instituted.

Fissures and abrasions are the least harmful, but also require special attention. Strict surgical asepsis and antisepsis are in order. Where an abrasion is clean, a dusting powder of dermatol or aristol is to be applied, but immediately to be substituted by wet treatment should evidences of infection, reddening, exudation and pain ensue. Fissures when in callous regions will heal most rapidly, if, after the edges have been softened by salicylic or soap salicylic applications (wet or plaster) these be pared down with a razor blade, so as to transform the deep cleft into a shallow wound. If the fissure be situated in an accessible region on the heel, margin of the foot (plantar aspect) and is absolutely free of infection, the plaster mentioned may be applied without hesitancy provided that it be removed and changed 2 or 3 times daily and the wound inspected for the possible development of signs of inflammation.

If there be a slight infection about or under a toe nail, the latter must be immediately cut in such a manner as to give free escape to secretions. Dressings (even wet) should *not* remain in contact for more than 1 or 2 hours at a time, and frequently saline foot baths (every other hour for one-half hour) will not only shorten the period of infection but encourage healing. Indeed, dressings of any kind over open wounds in these cases are dangerous unless they be very frequently changed, at least every other hour. Too much emphasis cannot be laid upon this statement; *for many a limb has been sacrificed to the traditional apathetic and disinterested attitude of the practitioner in the local treatment of these cases.*

Besides the measures directed to foster healing of such surgical lesions, the usual general treatment is applicable. The postural and hot air methods also have their place; the extent of their administration being a matter of judgment in each and every case.

3. *Cases with Chronic Ulcerative or Perforative (Perforating Ulcer) Lesions Without Progressive and Deep Infection (Phlegmons).*—Another, very valuable measure is at our disposal here, in the use of constant baths. Hot saline baths at temperatures from 95° to 105° F. are exceedingly valuable in these cases. Normal hyper- or hypotonic solutions of salt have been variously recommended. Indeed some would vary the concentration with the physico-chemical constitution of the blood serum of the particular patient treated. In general, slightly hypertonic solutions are advised. The baths are to be given either almost constantly during the day, or intermittently. Where infection has been kept in check, it is usually wise to alternate baths of 1 hour's duration with exercises and hot air treatment of similar length. The postural treatment is to follow the bath, and the bath to follow the dry thermal measures, in order to give the leg a chance to dry out before the heat is applied. Here, too, no inflexible rules can be laid down, for even the baths at body temperature, or the hanging position may be intolerable in certain instances. Should such be the case, an irrigation apparatus that flushes the parts with the foot at horizontal or almost horizontal is an apt variation of technic.

4. *Cases with Superadded Attacks of Thrombosis.*—We mean here particularly the sudden occlusive process in the deep arterial paths that may suddenly incapacitate the individual, or occasionally may be of slight symptomatic severity and only recognizable through the rapid alteration in the

objective state. In both, prophylactic treatment is to be carried out at once. The patient is to be put to bed, the affected part wrapped up in lamb's wool or other warm protective covering, guarded by special devices against pressure sores either at the heel, calf or toes. A wire cage or guard over the leg, covered by a blanket, enclosing an electric lamp or electric pad, will keep the part at whatever elevated temperature we may desire. Attention is to be directed to first, the state of the circulation during subsequent periods of each day and from day to day; second, the condition of the skin as to the effects of impoverished circulation for hemorrhages and lesions of impending necrosis; and third, for the arrival of that moment when active therapeutic measures for enhancing the circulation are to be initiated.

The severest effects of arrest of circulation are usually in evidence shortly after the onset of thrombosis with such manifestations as pallor, coldness, blueness, pain and insensitiveness of distal parts. There are cases, however, in which aggravation of circulatory supply occurs gradually *pari passu* with an advancing thrombosis, or through failure of collateral supply, or as a sign that irremediable damage has been done. Leaving the discussion of the latter two eventualities for subsequent paragraphs, we are concerned here with the cases that improve spontaneously and with our aid. As warmth of the part and color return, we begin to estimate the degree of ischemia, the angle of circulatory sufficiency and the extent of closure of the palpable vessels (pulses in the two pedal arteries, popliteal and femoral). The rapid advent, too, of rubor is a valuable and indeed prognostic sign of good omen. As soon as pain has abated, we can employ a greater amount of heat, although excessive heat is always to be avoided. Then we may begin, gradually with the postural treatment but in modified and restricted fashion, limiting the periods of elevation to a minimum, as well as the time of depressing and we may extend considerably the period of rest. Again, it should be remembered that very soon after the onset, the horizontal position may have to be avoided if pallor is evident at this level. On the other hand, stasis also is objectionable, so that services of an excellent nurse will be of unusual worth during this critical stage. Whenever it appears that the veins stand out too prominently with the leg at a slightly oblique decline, it should be lifted up for a moment to give the outflow its needed opportunity. Baths are to be scrupulously avoided, and the skin may have to be rubbed with coca butter or vaseline, since even water and soap may not be tolerated. The integument may become thin, atrophic and dry, and the oil applications are best borne. Minute hemorrhages and even small cutaneous necroses will often heal under dry treatment with non-irritating sterile dusting powders.

As improvement occurs, the postural method may be more vigorously applied. Care should be taken to keep the patient off his feet for weeks or even months. Sometimes this type is only a transition into the condition of chronic "phthisis of the leg" or "atrophic painful red leg," which may not tolerate ambulation for months, or which may permanently interfere with locomotion.

5. *Cases with Chronic Atrophy.*—Very little can be done in a therapeutic way for this type of case. Some develop gangrene, others remaining in statu quo for months or years. If locomotion be almost altogether interdicted, many limbs will be saved for the longest possible period and indeed life may thereby be prolonged.

6 and 7. *Cases with Gangrene with or without Infection.*—The various problems that confront us under these conditions have already been touched

upon, and it remains merely for us to apply the principles laid down to concrete clinical pictures.

Cases with Gangrene without Infection.—It need hardly be emphasized that no absolute restriction into such a category can be definitely prognosticated in any given case, since infection may ensue at any moment. Still within that period when there is gangrene of the dry or moist variety, the therapeutic procedures applicable are sufficiently uniform to permit of concise presentation.

In gangrene of the atherosclerotic variety, the treatment differs in essentials only as to whether complicating diabetes exists or not.

Gangrene without Hyperglycemia.—The patient is confined to bed and is given the general tonic and systemic treatments, that the cardiac and metabolic status warrant. The application of the kind and intensity of local treatment will have to conform to the site and extent of the gangrene. With dry gangrene of one or more toes, with a tendency to demarcation, an expectant attitude is best. The postural and hot air methods and the prophylactic measures previously alluded to, while the patient is in bed, on a couch or in a reclining chair, are excellent adjuvants in fostering limitation and demarcation of the process. Where, however, the gangrene is progressive and creeps over the dorsum of the foot, implicates several toes, and with the big toe involved ascends beyond the metatarso-phalangeal joint, the conservative methods will usually have to yield to radical surgery with ablation above the knee.

When signs of infection appear—tenderness in a direction proximal to the gangrenous digit be it dorsal or plantar, followed by reddish, bluish or purplish discoloration of the overlying skin—or if a drop of pus appears in the immediate vicinity of any trophic ulcer, the dry gangrene becomes for practical purposes of therapy, equivalent to the moist type, and the continuous (or frequent) administration of baths is in order. The concealed foci must immediately be opened by adequate incision under nitrous oxide gas. Or, anesthesia may be wholly dispensed with when cutaneous sensibility has been destroyed by the subcutaneous and subfascial disintegrating and putrefactive process. Undermined skin can often be incised without causing pain.

As the process becomes an infectious one, both postural and hot air treatments should be dispensed with; firstly, because they are difficult to carry out; and secondly, because they are attended with the danger of fostering extension rather than limitation of the infectious process.

When the latter reaches a certain degree of severity and extent, when lymphangitis is superadded, and when the limb is already seriously compromised, or, when the general systemic symptoms and signs of intoxication begin to appear, we should not tarry any longer, and forthwith advise amputation.

Gangrene with Hyperglycemia.—The problem becomes a more grave one here, and the state of the kidneys, heart, blood and urine must be carefully watched. The general medical treatment need not be dwelt upon other than to accentuate its great importance in determining the outcome. Not only must we estimate the sugar content of the blood, the presence of glucose, acetone and diacetic acid in the urine, and the CO₂ combining power of the serum or the alveolar air; but the blood chemistry as an index of the renal function must be given careful attention. For the prognosis is bad, when there is renal insufficiency, cardiac weakness and marked acidosis.

Of the many suggestions that have been made on the pre-operative treatment, the following seem to be the best: The administration of large

amounts of fluid, one glass every hour; thorough purgation with enemata; avoidance of fats that may increase acid production; and the administration of oatmeal, alcohol and levulose—substances that are said to favor the combustion of ketones.

Insulin.—The remarkable discovery of the therapeutic value of insulin (McLeod, Banting) bids fair to greatly improve the prognosis. Insulin may be administered hypodermatically for one or two days before amputation is contemplated and continued according to indications for a variable time thereafter.

Insulin is believed to be of great value both before and after operation. Although glycosuria may not disappear with its use, it is usually diminished and with the lessening of the glycosuria there is a fall in ketone bodies. Infection increases the gravity of diabetes; insulin lessens the danger of surgical intervention (Joslin).

To diminish the risks of acidosis and to limit the extension of this type of gangrene, we must intervene early to combat infection and especially the cold type of puriform gangrene that so insidiously creeps on through the deeper tissues. Tenderness, fluctuation, discoloration, boggy and puffiness must be sought for early and along the line of such objective signs, incisions must be made at timely moments. Digits should be removed as soon as they are gangrenous and tend to obstruct the adequate outflow of pus or gangrenous products that are apt to accumulate in the plantar aspect of the foot. The permanent or intermittent bath too, with or without use of the Carrel-Dakin solution is indicated.

The most valuable contribution to methods of treating this type of case was the discovery of insulin (iletin) which has justly found wide application in both the medical and surgical diabetic patients.

Surgical Treatment.—The more conservative methods have already been discussed, so that we may confine ourselves here to the utility of amputation.

Amputation.—Indication for amputation will depend upon whether conservative measures are successful or not, upon the general condition of the patient, and on the severity of the pain. It will, furthermore, be influenced by the rapidity with which the gangrene extends, and by the presence of a very extensive phlegmon that does not become arrested by conservative incision.

There seems to be no unanimity of opinion regarding just where and when to amputate in cases of this sort. In general we may say that when conservative treatment has failed—which includes methods of enhancing circulation, conservative incisions, dressings, and amputation of small extent—when gangrene shows evidence of progression, when no line of demarcation forms, and the suppurative process threatens the patient, then amputation above the knee, preferably at the lower third or middle is to be performed. This should be done under nitrous oxide anesthesia, by the circular method, the aperiosteal type of amputation being preferred. The femur should be cut high enough so as to avoid the production of a conical stump, when the flap retracts. Since we may expect slight sloughing of the periphery of the flap even in favorable cases, it is wise to make provision for this in advance. The wound should be left fairly wide open, although several catgut sutures may be placed into the muscles to bring them together and control bleeding. Sterile adhesive plaster may be employed to approximate the edges of the flap loosely, wide drainage until granulations have formed, giving the best results.

The results of amputation through the thigh are fairly good—as to mortality—in the non-diabetic cases, but the issue becomes progressively more grave in direct proportion to the age of the patient. In arteriosclerotic gangrene (even without hyperglycemia) any ablation below the knee is so dubious in its outcome as far as ultimate healing is concerned, that we recommend nothing but the high amputations through the femur. Such an intervention in the aged, needless to say, is sufficiently grave to awaken strong doubts in the minds of the immediate family as to the outcome; all the more so, since the high mortality of amputation in the neglected diabetic cases is a matter of common knowledge even amongst the laity. It is this attitude of the people and even of the average internist that is largely responsible for much neglect and procrastination, and indeed plays no subsidiary rôle in determining the eventual issue in a large percentage of the cases.

What shall be our attitude regarding the advisability of high amputation in a given case; and when shall we be warranted in deciding that local operative and restricted ablation of smaller parts (toes) will no longer suffice? The cases must be divided into the non-diabetic, young and old; and the diabetic, young and old, severe and mild.

The Pure Atherosclerotic (without hyperglycemia).—In the patients from 40 to 60 years (approximately) with good heart action, with renal adequacy and not too accentuated generalized atherosclerosis, we have been so well satisfied with the relatively low mortality of high amputation, that our fear of this operation will not deter us from recommending it at an early date. And so we are justified in resorting to it, when amputation of the big toe for gangrene, perforating ulcer or chronic trophic disorders does not avail, and a chronic suppurating sloughing wound with or without progressive gangrene—but with much suffering—results; also when a similar condition follows ulcers and gangrene of several of the smaller toes; or when with any local nutritional disorder, rapid, ascending infection, with or without lymphangitis and general toxicity occurs; or when there is massive dry gangrene of toes and a part of the foot; or when embolic or thrombotic processes lead to extensive dry gangrene of the foot and leg.

In the older individuals because of the high mortality, and the dubious local outcome of the wound through the thigh, our inability to promise much to the family and the prejudices previously alluded to, account for the even greater percentage of failures than we would otherwise expect, were high amputation conceded as best and permitted much earlier after the onset of the gangrene. Here, just as with the cases of “diabetic” gangrene (so-called) the author holds the view, that when once our clinical judgment tells us that the part can no longer be saved, amputation had best be done early, rather than late. For, the ensuing sleepless nights, the toxic absorption and continued suppuration are the factors that increase the mortality.

The Cases with Hyperglycemia.—In general we may say that here the intensity or gravity of the diabetes and the renal condition play a greater rôle in the outcome than the age of the patient. Attention has so often been directed to the excellent results following conservative treatment with limited amputation of phalanges or whole digits and multiple incisions for phlegmonous processes, that the physicians as well as the surgeons’ judgment and activities have become hampered, their ardor cooled, and their usual boldness converted into an attitude of apathy or even repugnance towards any radical measures. We cannot lay down rules by means of which the surgeon can conclude when the conservative incisions and other measures

will have failed. For, this is a matter of experience and clinical judgment. Exceedingly important as a prophylactic measure is the admonition, that the incisions above an area of gangrene or only threatening gangrene should not be delayed and all accumulations of purulent and gangrenous material prevented. When, however, with the most spirited form of local treatment the process is not arrested, or when by reason of massive gangrene naught is to be expected from such restricted measures, we believe that high amputation should be advised *as early as possible*.

We believe that the mortality could be considerably reduced by the exclusion of that immeasurable, indeterminate but still vital complex of deleterious factors that are engendered and accumulated by the ever growing infectious and gangrenous foci. Abolition of these toxic elements cannot be brought about by baths and incisions in many cases; although a diminution of their potency, it is true, is thereby attainable. Whilst conservatism may be appropriate in some cases, there are many in which despite such means, the above mentioned elements constitute a growing menace, cumulative in action, and determinative in upsetting a balance, which early operation might have been able to conserve.

With the prognostic sense of the surgeon well developed, and aptly and timely exercised into an expression of courageous conviction, and with the prejudices of the family overcome, many more lives could be saved by early intervention.

CHAPTER LXXIV

MISCELLANEOUS AFFECTIONS OF THE ARTERIES

For the sake of completeness, brief reference must be made to certain other less common vascular lesions with which necrosis or gangrene may be complications. These are (1) simple hypertrophy of the vessels that does not *per se* either cause internal or external necrosis or gangrene; (2) tuberculous lesions that produce such effects internally; and (3) aneurysms which may, especially through complicating thrombosis give some or many of the symptoms of the other obstructive vascular affections.

The following are the results of some of the more recent pathological investigations on arterial lesions.

Pathology.—In a general way the non-traumatic lesions of blood vessels are referable¹ to (1) disturbances of nutrition; (2) disturbances of growth and development; (3) toxic effects; (4) infection (bacterial in general); and (5) special infectious agents.

1. *Lesions of Disturbed Nutrition.*—When the blood supply is partly or completely in abeyance, alterations in the vessel wall may take place. Such changes are usually of embolic or thrombotic nature. The elements of the vessel wall may undergo necrosis, or (in anemia) may show the presence of fat, hemorrhage and weakening of the walls.

2. *Disturbances of Growth and Development.*—Here belong atrophy, regressive changes, and hypertrophy. The latter will receive more detailed discussion later, since this pathologic process may be of some importance amongst the changes that occur in the arterial affections of the extremities.

¹ In part of this grouping the divisions suggested by Mallory have been adopted.

Atrophy may result as a senile change with spontaneous disappearance of the mural elements including elastic fibers and muscle cells with substitution of connective tissue. Usually such change is more apt to follow occlusion due to thrombi when the wall of the vessel may become converted into connective tissue, and even become hyaline. Other regressive changes, including sclerosis calcification, fatty degeneration, concern us here, only in so far as they form a part of the process elsewhere described as athero- and arteriosclerosis.

3. *Toxic Lesions*.—These may attend the infectious processes, and have a special affinity for the arterial system. Diphtheria, scarlet fever, pneumonia, streptococcus infection—all are believed to produce toxins that may injure



FIG. 148.—Artery—heart. Acute infectious lesion; necrosis, fibrin formation, leukocytic infiltration; yielding of wall forming infectious aneurysm. (Mallory.)

the vessel wall, cause fatty degeneration of the cells, hyalin change or necrosis. Often there is a tendency to focal distribution, which cannot be explained, and, according to Mallory, is not dependent upon the *vasa vasorum*.

4. *Infectious Lesions*.—These depend upon the immediate presence of pathogenic organisms. The histologic alterations vary with the type of infecting organism. There may be acute lesions due to the pyogenic organisms, with destruction of vessel wall and abscess formation; or, when the organisms are less virulent and die off readily, less intensive lesions are produced.

Infection of the blood vessels may take place from without by continuity or through the adventitia and *vasa vasorum*, or from within. The inflammatory reaction on the part of the blood vessels is said to be due either to the organism itself, the toxin derived therefrom, or to the injured cells.

Leukocytes may accumulate under the endothelium of the blood vessel in acute infectious processes and especially as the result of the action of the

glanders bacillus. Endothelial leukocytes and lymphocytes may accompany them.

Mallory believes that the resulting formation of fibrin when undissolved by ferment and not eliminated, may cause proliferation of fibroblasts. In this way thickenings are produced that may be of injurious nature. An excellent example of infectious lesions in an artery from the heart of a case of streptococcus infection is seen in Fig. 148. Here a focal infection of the wall with necrosis, fibrin formation and leukocytic infiltration is depicted; the wall at this point shows the beginning of the development of an infectious type of aneurysm.

5. *Special Infectious Agents*.—Here may be mentioned the results of blood vessel infection due to certain organisms that bring about lesions of special types. These are the glanders, leprosy bacillus, the treponema pallidum and the tubercle bacillus. The lesions of the last two are discussed in special sections. The pathological process of periarteritis nodosa, probably of infectious origin is also separately described.

CHAPTER LXXV

HYPERTROPHY OF THE ARTERIES

Although this affection does not lead to gangrene, we should be aware of its existence, since it may accompany diseases that are thus complicated. One of the forms of hypertrophy affecting arteries that has been confused with obliterating endarteritis, gives pictures that have oftentimes been mistaken for the end products of organization of thrombi. For purposes of differentiation, therefore, it is well to know something regarding these hypertrophies or obliterative changes springing from the intima.

Hypertrophy of the arteries may be a functional response, and difficult to differentiate from pathological conditions. The process may affect vessels active in collateral circulation, as well as the new formed and old vessels in neoplasms. In chronic hypertension hypertrophies of isolated portions of the vessel wall may take place. Proliferation of the muscularis and new formation of the elastic fibers are described.

Hypertrophy of the connective tissue within the vessel wall is of pathological significance. A slight degree of proliferation of the connective tissue in the intima is considered to be physiological. The endothelium (which in the foetal vessels lies directly against the internal elastic coat) is gradually displaced by proliferation of cellular connective tissue as time goes on. At first this connective tissue shows no tendency to the formation of sclerotic lamellæ. This proliferation is considered as a regenerative process in substitution for interruptions in vascular continuity. They are seen where cicatrices follow traumatic lesions. As a compensatory process proliferation here may occur in many diseases of the vessel wall, and goes on so slowly and constantly, that it is not observable until the finished product is striking. Again, proliferation of the intima is also regarded as a disease *per se* in cases in which no cause can be found.

The process seems to proceed in the following manner. Although it was first believed that the cells appearing between the endothelium and elastic

coat are derived from the endothelium, it is now generally accepted that the fibroblasts may have their origin in the deeper layers of the vessel wall, penetrating the fenestra of the elastica. At first stellate and spindle celled elements appear. Then the loose connective tissue becomes denser and lamellated. If degenerative processes are absent, then this tissue develops elastic fibers and its own elastic system.

In this way a tissue is formed that serves as the chief element in resisting dilatation of the vessels. Such tissue increases the central resistance (resistance to distension) of the vessels, and is unable to accommodate itself to the varying size of the lumen, as the normal vessel tissue can. It therefore acts as a distinct obstructive element to the circulation.

In short, a sclerotic process in the vessels is thus formed, that leads to partial obliteration, particularly in the smaller ones, where it is regarded as an obliterating endarteritis. It is not believed that this productive process is a disease *per se*, but the response to numerous different provocative processes.

CHAPTER LXXVI

ACUTE ARTERITIS

Acute arteritis affects either the visceral arteries, the arterioles, or the larger arteries, such as the aorta and those of the extremities. When it follows infectious fevers it is not apt to be generalized, but tends to be limited to certain territories.

The subject of arteritis has received relatively little attention. We are concerned here especially with those lesions that are believed to produce peripheral circulatory disturbances either immediately, during the acute stage of the process, or subsequently by reason of thrombosis or other secondary mural changes in the arteries.

The investigations of Wiesel on the arteries during the course of infectious diseases—such as diphtheria and scarlet fever—have demonstrated that distinctly recognizable alterations in the vessels occur. In the course of these maladies the changes manifest themselves in the form of a degenerative process in the smooth muscle and the elastic fibers. Usually the process begins in the media and is for the most part confined to this coat. The degeneration is focal, may occur in numerous situations and lead even to veritable necroses of the vessel wall in the severe cases. Such necroses may heal with resulting cicatrices, or a return to the normal may take place. When the intima is involved, permanent alterations occur. Even macroscopically recognizable lesions may develop.

Any of the arteries of the vascular system may be affected from the largest to those of the caliber of the digital arteries. Two groups have been described: (1) processes with marked participation of the elastic elements (diphtheria, typhus and pneumonia, influenza); and (2) those in which the musculature is particularly implicated (as in scarlet fever and septic diseases).

The changes here described are not those of beginning arteriosclerosis. Distinguishing features of arterial lesions in the acute infections are the primary localization in the media, and confinement to this layer in most instances. Nor do the arterial lesions of syphilis usually begin as an infecti-

ous arteritis. But in the experimental vascular lesions produced by adrenalin injection into animals, the characteristic change is often a primary necrosis of the smooth muscle and the elastic elements of the media. Intima changes are secondary or late. In this respect the arterial affections of the acute infectious processes resemble that of the experimentally produced arteriosclerosis.

Etiology.—Acute arteritis of the extremities usually complicates the period of convalescence after typhoid, influenza, cholera, and scarlet fever. In typhoid fever the inflammation of the arteries is said to appear about the end of the third week, or even later, and may be attended with thromboses. Gangrene of the extremities may result by reason of the accompanying complicating obturating thrombosis, although in some of the reported cases embolism may have occurred. The lower extremities are those usually affected, more commonly unilaterally; and the femoral, popliteal, posterior tibial, more rarely the external iliac and anterior tibial or pedal arteries are affected; in the upper extremity, the brachial artery.

Influenza is next in frequency as a cause of acute arteritis. Here the femoral and popliteal arteries are most often affected; then the brachial and axillary. Gangrene has been observed in about two-thirds of the cases. In *typhus* fever also, gangrene due to arterial changes and thrombosis is not uncommon, the femoral artery being usually diseased.

In acute articular rheumatism, the aorta, carotid, axillary, and brachial arteries are described as being the seat of arteritis. Even aneurysms of the posterior tibial and radial may be developed. Some authors account for the lesions in this malady rather as due to an embolic process than to primary affection of the arterial walls themselves. And so, the cases of gangrene described are, therefore, interpreted as resulting from thrombotic or embolic occlusion. Gangrene of the extremities complicating arteritis may occur with puerperal infection¹ and pneumonia. Similar observations have been made in scarlet fever, and thrombosis of the popliteal is reported in cases of smallpox.

Even in erysipelas during the convalescent period thrombosis of the popliteal may be a complication; in cholera it is not infrequent to find gangrene due to arterial thrombosis. Similar observations have been made in dysentery, appendicitis, peritonitis, angina and gastroenteritis. In advanced tuberculosis thrombosis of the arteries has been reported involving the extremities with the brachial, subclavian and tibial arteries affected.

Pathology.—There may be localized thickenings of the intima with limited or circumscribed prominences (Roger and Gouget). In these there is cellular proliferation beneath the endothelium with various types of cells; one being large connective tissue cells with processes, another type, more numerous, consisting of round cells. In cases where the lesion is more intense, the middle coat may be affected, but usually to a lesser degree. The internal elastic lamina or membrane may be irregular and fragmented, and leukocytes surround new formed capillaries. The latter have their source in vessels that penetrate from the external coat, causing a certain amount of disintegration of the muscular and elastic fibers of the media. In some infectious diseases the lesions of the middle coat may predominate (diphtheria, typhoid, grippe, scarlet fever, rheumatism); and Wiesel describes necrotic foci.

The external coat is said to be either uninvolved, or the first to be affected. Inflammatory processes in the vasa vasorum with perivascular leukocytic

¹ Wormser, Wien. klin. Rundschau, 1904.

infiltration and proliferation of fixed cells have been noted. However, all three coats may be eventually implicated.

In a general way the lesions are similar to those of acute aortitis, except that in the latter the intima may appear intact, and smooth, but covered with gelatinous plaques and without thrombosis. In the arteries of the extremities, however, the clotting process is more apt to occur by virtue of the smaller size of the vessels and the retardation of the blood stream.

Usually a clot will adhere to the affected region, at times insufficient to obliterate the artery; but more frequently secondary clot formation (accretion, stasis or stagnation clot) leads to obliteration of the artery, with extension of the thrombotic process towards the periphery (also centrally) and even into branches. By reason of the rapid extension of the clotting or the thrombotic process it is difficult or often impossible to distinguish the primary seat of the clot formation. Only at autopsy is this possible, when a more nearly correct appraisal of the age of the thrombus can be made macroscopically and microscopically. Organization of the clot usually follows.

As a result of thrombotic obliteration, *gangrene* has been observed in the extremities, and *infarction* in the internal organs.

Symptomatology.—Although arteritis may involve the visceral arteries, we are concerned here merely with those of the extremities. The best opportunity for studying the symptoms of this malady is offered in the course of infectious diseases. The following description given by Roger and Gouget is typical of the acute manifestations of arteritis of the peripheral vessels:

Although the manifestations may begin without apparent cause, their inception is usually referred to an untoward or brusque movement. The patient experiences sudden pain in the affected limb along the course of one of the larger arteries. The pain may be localized, may radiate throughout the limb, is intensified by motion, and tenderness can be elicited along the course of the artery (usually in the axilla, in Scarpa's triangle, Hunter's canal or in the popliteal space). Increase of temperature usually occurs simultaneously with or immediately after the onset, and also, sensory and circulatory disturbances in the peripheral parts.

At first, paresthesia, formication or intense pain in the toes and calf of the leg are experienced. The pulses below the point of obliteration may be absent or diminished, some of the arteries being converted into hard painful cords. The symptoms vary with the site of the obstruction and the artery involved. Then the usual symptoms common to arterial blockage may be evolved; and even *gangrene*. Usually, however, the collateral circulation is sufficient to prevent extensive mortification. An intermittent course was reported by Eichorst and Mornet, in a case of arteritis due to influenza. In this instance the affected limb was found cold and partially anesthetic, the pulses imperceptible on one day; and on the morrow improvement took place with increased warmth, restored sensibility and pulsation. Then again, there was a recurrence finally followed by gangrene.

In some cases the course is a rapidly progressive one, as if an embolic lesion had occurred: suddenly the patient experiences a tearing pain, the affected member becomes pale and cold, and gangrene is the issue.

In an interesting clinical observation which was regarded by Dr. E. Libman and Dr. I. Strauss as one of arteritis following scarlet fever, there was a history of sudden cramp in the legs, both becoming cold, white and ischemic, in a child 5 years of age, 9 days after the beginning of the disease. There appeared to be no circulation below the knees; there was pain in the right great toe; but the circulation was restored during the following 24 hours.

About this time there was a right sided hemiplegia which was referred to a similar process in the cerebral arteries.

Rheumatic Arteritis.—The literature affords sufficient data to warrant the view that inflammation of the arterial wall may occur with rheumatic infection. In the aorta the intima has been found to present yellowish plaques of a gelatinous nature, occupying a part or the whole circumference of the vessel wall of the aorta and large vessels. Such areas, when situated in vessels of smaller caliber, may produce considerable narrowing and predispose to secondary thrombosis. Later, degenerative changes and calcification may convert such plaques into areas indistinguishable from atherosclerotic patches.¹

Microscopically the lesions of the intima comprise proliferative changes in which the connective tissue cells with some leukocytes play the most important rôle. The cells are sometimes described as of embryonic type. The endothelium covering the plaques is intact in most cases.

Characteristic changes have been noted in the media. The muscle fibers suffer the most intensive alteration. These show degenerative changes, and may disappear altogether leaving only the elastic fibers and a few degenerate nuclei and polynuclear cells. These necroses have been attributed to the toxins of rheumatic infection.

As for the adventitia, a periarteritis is described and is believed to play an important rôle in the sensory symptoms.

Symptomatology.—In view of the common incidence of rheumatic fever, acute lesions of the arteries are rather rare. The following arteries may be mentioned in order of decreasing frequency of involvement: the aorta, the carotid, the brachial and subclavian, the axillary, and the coronary. Least frequent of all, is the involvement of the vessels of the lower extremities. In this regard this affection is distinguished from the arteritis complicating typhoid and other infections in which the arteries of the lower extremities give most frequent evidence of disease.

The first manifestation that attracts the notice of the clinician is the *pain*, which is constantly mentioned in all reported cases. It is spontaneous, localized in the region of the affected vessel and the least contact with the latter may augment and markedly intensify the suffering; sometimes acute exacerbations of paroxysmal nature may occur.

A moderate degree of fever and increased rapidity of pulse may accompany. The French authors speak also of an exaggerated pulse in the arteries, and attribute it to a dilatation of the vessel through muscular relaxation. Later, however, this gives way to diminished pulsation, due, in the case of the smaller arteries, to narrowing of the lumen. Sometimes, however, dilatation of the arteries is observed. Even an arterial murmur has been described as audible over the vessel. These are the symptoms referable to arteritis without obliteration, a type of arteritis described as *parietal arteritis*.

In the *obliterated arteries*, the radial pulse may completely disappear, and the arteries become transformed into hard fibrous cords. There may be associated coldness of the peripheral parts (usually the hands). Later, the affected member becomes pale, flaccid, diminishes in size, the hand becomes atrophied, and the nails show dystrophic changes. Sensory disturbances with diminished sensation to heat and pain are attendant symptoms.

Clinical Course and Prognosis.—In the benign forms, spontaneous cure occurs, and after 2 weeks the pain disappears, the arteries returning to normal.

¹ Offering plausible basis for the infectious theory of the pathogenesis of atherosclerosis.

At other times there is a tendency to multiple invasion of arteries, the patient finally succumbing with cerebral symptoms.

When an obliterating arteritis develops, *dry gangrene* of the part may possibly be the issue. Definite cases of such gangrene are not reported, although imminent mortification and trophic disorders appear in the reports in the literature. Other eventualities are aneurysmal dilatation or a chronic arterial change that leads to arteriosclerosis.

*Rheumatic phlebitis*¹ may appear after the articular manifestations. With sudden onset, sometimes preceded by chills, malaise, and elevation of temperature, it may have a migrating tendency, and affect numerous veins in different parts of the body. Just as in the case of the arteries, there may or may not be obliteration of the veins. A late edema of the peripheral parts is observed in some cases. Out of 27 cases observed by Schmidt, the lower extremities were involved 15 times the upper once; in one case the veins of all 4 extremities were implicated. These observations are in contrast to those of rheumatic arteritis where the upper extremities are most frequently affected.

Acute Arteritis of Unknown Origin.—In an interesting recent communication, Kramer² describes a case of gangrene in a child, due to arteritis with thrombosis and not preceded by a definite infectious disease. The clinical picture at the onset was that of purpura of either the hemorrhagic or fulminating type. There was a sudden onset, injected throat, leukocytosis, then purpura, extensive ecchymosis and finally gangrene of one leg; the patient recovered after amputation, and the nature of the infectious process responsible for the arteritis could not be determined.

E. H., white, male, 8 years old, was admitted December 7, 1920 (Dr. Solis Cohen's service) with a provisional diagnosis of purpura. One week previously the boy complained of headache, became restless and feverish, and vomited twice. The patient was very pale. Two days later purple blotches appeared on the knees and outer aspects of both legs and later, on the body as well.

Physical examination revealed an injected pharynx, enlarged and injected tonsils. The extremities showed ecchymotic patches with sloughing. The left leg was the worse, the foot being blue, the toes cold and bluish black in color. No pulsation of the dorsalis pedis could be discerned. The temperature on admission was 99° F.; later it went up to 104°. The pulse range was from 90 to 110. There was leukocytosis 26,400; polymorphonuclears, 81 per cent. The blood culture was sterile. The throat culture showed streptococci. The patient's condition became steadily worse. Gangrene developed in the left foot.

Amputation was done above the knee on December 31, about three and one-half weeks after the patient's admission. Convalescence was slow, but recovery finally ensued and (January, 1922) the lad was robust and enjoying good health. The limb was studied by the histologist, Dr. W. P. Belk, who reported as follows.

Pathological examination. The large arteries showed a thickening of the media, which was due to a moderate proliferation of fairly young connective tissue cells. There was also a moderate amount of round cell infiltration in this arterial coat. At one point one large artery showed what appeared to be a very early and *slightly marked necrosis*. Opposite this there is a thrombus firmly attached to the intima. The endothelial coats at this point have been lost.

In all sections the small arteries showed a more advanced pathological process. The thickening—still chiefly of the media—was great, resulting in the narrowing of the lumina to about one-third or more of the original diameter.

It is quite conceivable and doubtless true that arteritis of unknown etiology, may be responsible for some of the phenomena of disturbed circulation occasionally encountered during adult life. For, gangrene is not always the immediate issue but occluded vessels may predispose later in life to circulatory deficiencies whenever the vascular paths become still

¹ See Chap. LXXXI, Miscellaneous Varieties of Migrating Phlebitis.

² Kramer, New York Med. Jour., Oct. 4, 1922, p. 394.

further compromised. Such added lesions may be bland thrombosis, thrombo-angiitis, arteriosclerosis and some of the other obstructive processes elsewhere described.

In a study of other sections¹ the author found that in one of the larger arteries a large area of necrosis occupies a fair portion of the wall involving all of the coats. The muscle cells showed extensive degeneration. The presence of wandering cells suggested that an inflammatory reaction had been present, at least at the onset, in this zone. The immediately adjoining portions of the arterial wall show the most intensive proliferative reaction (Fig. 149).



FIG. 149.—Arteritis with mural necrosis; above, there is a zone of necrotic wall, bounded on the right by vascularized, inflamed media; below, occluding clot. (*Kramer and Krumbhaar*)

In this area bordering on the necrotic portion there is edema and slight degeneration, proliferation of all of the cells, and separation of the muscle fibers partly by the new formed capillaries. In other portions of the arterial wall, numerous new formed capillaries run in a more or less circular direction thereby causing thickening of the arterial wall, the process diminishing as we trace it away from the necrotic zone. Inasmuch as these changes are intensively present where the occluding clot still shows no evidences of organization, it is fair to assume that they are the response to the primary changes in the arterial wall (the so-called arteritis). From the sections at hand it would seem that these primary alterations were a combination of focal necrosis and inflammation, and that the lesion seen in the section (taken from the leg 3 weeks after the onset of the disease) represents rather the attempt at healing than a specific inflammatory process *per se*.

¹ Received by author through the courtesy of Dr. Kramer and Dr. Krumbhaar.

Arteritis with Thrombosis Simulating Thrombo-angiitis Obliterans.—Symptoms identical with thrombo-angiitis obliterans, but with a different clinical course, confined to one of the upper extremities, may present a clinical picture the classification of which may be difficult or impossible. Manifestations including all the symptoms of impaired circulation, with occlusion of the brachial, radial, or ulnar arteries, trophic disturbances, ischemia or rubor, may follow insidiously after a history of acute infectious disease (influenza). Without reliable clinical observations the relationship between the previous infection and the occlusive condition of the arteries may not be clear.

In short, symptoms identical with those of thrombo-angiitis obliterans, but of rather rapid development, confined to an upper extremity may be the evidences of occlusion of the large arteries, the result of either an acute arteritis with thrombosis, or acute thrombo-angiitis obliterans. The following case may be of interest.

T. C., Italian female, 29 years of age, suffered an attack of influenza in January, 1922, after which variations in temperature of the right upper extremity were noted, most marked in the index and middle fingers. The color of this extremity was inconstant, varying from a dusky hue to red and white. One week after plunging the right hand into warm water (December, 1922) because of its constant cold feeling, an ulcer appeared at the tip of the middle finger.

Physical examination, January 29, 1923, reveals general atrophy of the right hand and forearm. The tips of the fingers of the right hand are discolored, and an area of necrosis over the tip of the middle finger is in evidence. The fingers have a tapering appearance, due to tumefaction of the interphalangeal joints. There is ischemia of the right hand upon slightest elevation, reactionary rubor in the pendent position.

The right radial and ulnar pulses are imperceptible; also the right brachial below the first inch of its course.

The pulses of the left upper extremity are present; no evidence of any disturbance in the lower extremities.

Pathogenesis.—It is believed that arteritis may result from 3 different causes; firstly, from the bacteria which have caused the primary malady (acute infectious disease); secondly, from a secondary invader; or thirdly, through the effects of toxins. The bacteria which are believed to be commonly responsible for arteritis are the typhoid bacillus, the pneumococcus, and streptococcus. Often a secondary invader is said to provoke the lesions. Those who lay stress upon the effects of toxins on the arteries mention the lesions in the smaller vessels (arterioles of the viscera) as examples.

It has been a mooted question as to whether infection of arteries takes place by way of the *vasa vasorum*, the lymphatics, or directly through contact with the streaming blood. A review of the work of Wiesel and others, and a study of the material in the case of Kramer, would lead to the conclusion that at least in some of the cases of acute arterial disease complicating acute general infection, focal necroses attributable to impaired circulation in the arterial wall itself, or embolic processes in the *vasa vasorum* must be responsible. A reference to Fig. 149 will show the extent of the necrosis in the artery, the reaction immediately about it in the adjoining arterial wall, and the intact condition of the internal elastic membrane. Here an embolic agent whose portal of entry is through the *vasa vasorum* seems to offer the most plausible explanation of the degenerative lesion.

CHAPTER LXXVII

TUBERCULOSIS OF THE ARTERIES

Two distinct forms are recognized. In one the arteries are involved by propagation from the vicinity (secondarily); in the other they are the seat of embolic, or metastatic infection from a distance.

The first of these need not be discussed here, since it does not concern the vascular derangements of the extremities. It will suffice to point out that the arteries are involved in the tuberculous process in all chronic tuberculous foci.

As for the second type, it has been shown¹ that the following arteries may be thus affected: the meningeal, the renal, the pulmonary artery, the aorta, the brachial and subclavian, the iliac and the femoral. The tuberculous inflammatory processes in the arteries occur in the form of periarteritis and endarteritis.



FIG. 150.—Tuberculous periarteritis and aneurysm of pulmonary artery. A, Afferent artery; B, efferent artery; C, lumen of the aneurysm. a, Media; b, internal elastic lamina; c, external elastic lamina; d, diffuse proliferation of intima; e, margin of point of arrosion of media; f, margin of point of arrosion of elastica externa; h, proliferation in intima; i, aneurysmal dilatation of the hyalin intima; j, cheesy masses. (Benda)

Periarteritis is noteworthy in the arteries of all tuberculous foci. A concomitant proliferation of the intima leads to narrowing that is sometimes followed by thrombosis and obliteration of the lumina. The inflammatory process advances from the adventitia through all the layers to the intima, and is accompanied by leucocytic and lymphocytic infiltration.

¹ Orth, Marchand, Weigert, quoted by Roger and Gouget, *Maladies des Artères*, Bailliere, 1915, p. 143.

In this way the arteries are converted into solid cords that resist the tuberculous degeneration for a long time. When end arteries are affected, nutritive disturbances of the organs supplied by them occur. So, in the brain, anemic foci with softening may result from tuberculous periarteritis. More rarely, when larger vessels are involved, the tuberculous periarteritis may penetrate into the lumen, causing local or general dissemination of bacilli, as in the kidneys. Usually, however, the inner layers of the artery become hyalin, may be forced to protrude by the blood pressure, forming a sort of aneurysm, and usually leading to perforation. This occurs in the lungs, and is the anatomical basis for lung hemorrhage.

Tuberculous endarteritis is rare. It is seen in the form of solitary or multiple polypoid tubercles in the aorta or large arteries, either springing from the smooth intima, or from atheromatous foci. These polypoid masses are composed superficially of necrotic and thrombotic masses, whilst deeper, where they are attached to the intima, granulation tissue containing giant cells and bacilli are found. Tubercles of the intima of arteries are rarely seen (Fig. 150).

Obliterative lesions are rather rare in the arteries of considerable size. But thromboses of pulmonary arteries are reported. And Bäumler describes venous and subsequent arterial thrombosis occurring in both lower extremities in a young patient afflicted with tuberculous pleurisy. In spite of amputation the patient succumbed. Histological examination showed tubercles in the walls of the thrombosed arteries (Ménétrier).¹

CHAPTER LXXVIII

SYPHILITIC ARTERITIS AND GANGRENE

There are authentic cases in the literature of gangrene of the extremities with primary arterial luetic lesions as the cause. It is not always easy to glean accurately from the perusal of recorded cases as to whether gangrene is due to primary acute, or to slow, obstructive changes in the vessels, to secondary thrombosis, or to recrudescing luetic involvement of collateral paths in cases in which circulatory impairment has already been present for some time. However, an exposition of the facts at our disposal with a description of the various arterial lesions is important for an understanding of our theme.

Pathology.—The *smallest* arteries participate in every gummatous inflammation to such an extent that in all probability, the typical necroses are rather the result of nutritive disturbances due to arterial lesions, than to the action of specific toxins. The smallest vessels may show complete closure of their lumina, and various degrees of encroachment upon their patency due to thickening of the intima. Cellular infiltration of the adventitia usually accompanies an intact media.

In the *small* arteries there is an absence of those calcareous deposits and macroscopic necroses seen in arteriosclerosis. In recent cases the *inflammation involves the adventitia only*. Here there are foci of small cell infiltration, usually lymphocytic, with occasional leukocytes. Sometimes the latter are present in large numbers, particularly about areas of necrosis at the boundary of the media. The intima is very intensively diseased. Some of the thickening of the intima is doubtless due to a compensatory regenerative

¹ Ménétrier, Arch. de méd. exper., 1890. Cit. by Roger and Gouget.

proliferation. With this, there may be thrombosis. In severe cases the small cell infiltration may be associated with giant cells and necrosis, involving the whole of the vessel's circumference. The media is relatively more resistant, and may be partly free at a time when the intima already shows gummatous foci, and leucocytic infiltration. The lumen becomes closed through intima proliferation (Fig. 151), and partly through thrombosis. With the infiltration of the intima, there is interruption in the elastic lamina that are destroyed in a passive manner, and *do not proliferate as in atherosclerosis*.



FIG. 151.—Gummatous panarteritis (cerebral); *a*, adventitia in media with large gummatous infiltration; at *b*, giant cells; *c*, internal elastica, lamina split by gummatous infiltration into several lamellae; *d*, perforation of elastica; *e*, compensatory proliferation of intima; *f*, small gummatous infiltration of intima. (Benda)

During the healing process, the cellular infiltration of adventitia and media disappears, and the intima proliferation shows connective tissue replacement. New formation of elastic tissue may then follow.

The features are, therefore, first, cellular and gummatous infiltration with or without necrosis; second, destruction of the elastic lamellae; third, giant cell formation near the internal elastic lamina; fourth, giant cells outside of the vessel wall; fifth, proliferation of the intima; and sixth, secondary thrombosis (Figs. 151 and 152).

If we compare these findings with those in thrombo-angiitis obliterans, we will note that the striking differences are the presence here of giant cells outside of the vessels, the destruction of the elastic tissue, the proliferation of the intima, the foci of gummatous infiltration, the necroses of portions of the vessel wall, and the type of thrombotic organization.

According to Rosset¹ the lesions of syphilitic polyarteritis vary considerably, the arteries being sometimes converted into hard cords, sometimes

¹Thèse de Paris, 1920.

calcareous. The caliber of the artery may be simply narrowed, the lumen remaining more or less circular. Or there is a parietal endarteritis, the lumen of the vessel being deformed. In certain sections complete obliteration has been observed, due either to hyperplasia of the walls, or to thrombosis at the level of a plaque of arteritis. Above the point of stenosis, the caliber of the artery may be augmented; the narrowings may be few, or multiple over long stretches of the vessel. In the stenosed areas lesions may be absent or minimal; or occasionally there may be slight dilatation.

Microscopically the intima is particularly involved, the external and middle coats being relatively intact. The subendothelial coat is 4 or 5



FIG. 152.—Recent gummatous periarteritis (cerebral); *a*, intima proliferation; *b*, inflammatory infiltration in the outer margin of the intima with a giant cell; *c*, elastic limiting lamella interrupted by leukocytic infiltration; *d*, media with small foci of leukocytes; *e*, adventitia with large gummatous infiltration; at *f*, necrosis. (*Benda*)

times the normal size, thickened by virtue of concentric layers of numerous fixed connective tissue cells. The internal limiting elastic membrane is interrupted in a number of places by new formed tissue of vascular type, originating in the media. The intima presents protuberances due to rounded vegetation, which may project into the lumen.

The media shows very little although the muscular tissue may be atrophied. The adventitia is thickened, and there is distinct periarteritis that may extend to the accompanying veins.

The lumen of the vessel may be obstructed by clots which show various stages of organization.

Druelle divides the lesions into 3 types. The *first* is one in which there is a panarteritis with all of the arterial coats involved. It may be acute, and offer a fulminating clinical picture; or chronic, when it constitutes the anatomic substratum for ectasis and syphilitic aneurysm. The *second* type shows the lesions of endarteritis. This process is said to lead to sclerosis, but not to gummata. As a result, narrowing and even obliteration of vessels takes place, and hence, an endarteritis obliterans of sclerotic variety. The

third is an arteritis and periarteritis with gummatous changes in which the alterations in the adventitia are more marked than those in the intima, both as regards intensity and extent. Veritable gummata appear in the arterial walls, and have been demonstrated in the vessels of gangrenous limbs. Secondary thrombosis is often an accompanying lesion that leads to the usual complications. It may be concluded from this exposition that in the first two types a positive differentiation from other arterial affections cannot always be made.

Since the larger arteries of the extremities, especially the tibial, femoral and brachial arteries, when the seat of old luetic lesions may not offer anything absolutely characteristic, the following points have been suggested as of differential value: the predilection of the disease for certain localities (central nervous system); the symmetrical distribution; the circumscribed nature of the lesion in the vessel wall; the predominance of the proliferative over the regressive degenerative changes; the tendency to form nodules that resemble gummata; the rather rapid development of the lesions; and the relative youth of the patient.

In the aorta the adventitia and media seem to be the chief localities for luetic disease. In the intima there is compensatory proliferation; it is involved only in the most intense degrees of specific infection and necrosis. In the cases of recent activity true gummata may be recognized. There are lentil-sized or larger yellowish necrotic foci. They can be differentiated from those of atherosclerosis by the gelatinous thickening of the surrounding adventitia, and because of the penetration of the necrosis into the adventitia. Small irregularities of the intima with corresponding depressions and defects of the media are characteristic in the earlier stages; but later on the macroscopic diagnosis may be impossible. Cicatricial retraction of the intima with attenuation of the coat has been observed. However, inasmuch as arteriosclerosis may show a cicatricial form, a differentiation may be well nigh impossible. Therefore, here again only the finding of gummatous foci, cellular infiltration with necrosis and giant cells are dependable criteria for diagnosis of luetic disease.

The finding of *spirochætæ pallida* in the non-gummatous form is a recent contribution worthy of note. Benda¹ reports the presence of numerous spirochætes in the adventitia (also Strasmann²).

Incidence.—Instances of gangrene of the extremities as a consequence of syphilitic arteritis are of infrequent occurrence. Of 14 cases (Druelle³) only 2 were over 50 years of age. The gangrenous process is of the dry variety, not unlike that of senile gangrene. As to the time that elapses between the onset of the syphilitic infection and the onset of evidences of arterial complication and gangrene, weight of opinion leans to the view that it is a tertiary manifestation. Nevertheless, there is a precocious form that appears during the secondary phase of the malady (2 years after the chancre in the case of Fournier). In it, gangrene is described as the sequel of an acute arteritis; and during this period the chancre may be still present. These cases belong to a fulminating or malignant precocious form of arterial affection.

Males are more frequently affected than females, there having been 1 female in the above series of 14. As for the lesions, the late alterations in the vessels need not be wholly due to syphilis, but may result from a number of complicating factors, amongst which those leading to atheroma, atherosclerosis, alcoholism, and renal disease play a rôle. This association of multiple causal moments makes it often difficult to interpret the nature of the arterial disease. Nevertheless, certain undoubted syphilitic lesions in arteries have been recognized.

¹ Benda, Aschoff, *Pathol. Anat.*, 1919, p. 86.

² Strasmann, *Beitr. z. path. Anat.*, 1910, 49.

³ Druelle, *Thèse de Paris*, 1906.

Symptomatology.—We shall discuss here merely the symptoms when arteries of the extremities are involved, although it must be remembered that intestinal forms of syphilitic arteritis are described as giving rise to painful crises, the analogy of intermittent claudication. Intestinal infarction with a clinical picture resembling that of mesenteric thrombosis has been reported.

There are very few, if any, distinctive features that will differentiate the symptoms brought on by syphilitic disease of the vessels of the extremities from occlusive lesions due to other causes, such as atherosclerosis or thrombo-angiitis obliterans.

The onset may be insidious and progressive, with weakness and heaviness of the affected extremity. The sensations of cold, formication and vague pains are described. Or the onset is sudden with severe violent pain in the lower extremities, causing the patients to stop in their walk. The affected limb may become livid, and the pulsations feeble. This picture is comparable with that described elsewhere as due to sudden thrombosis in arteriosclerosis and thrombo-angiitis obliterans.

At the beginning the dominant symptom is pain which may be lancinating, prevent sleep, even necessitating injections of morphine. Whilst this pain may be diffuse at first, it is apt to be localized in the neighborhood of one of the toes later on, particularly when trophic ulcers or wounds appear.

Discoloration of the skin of the foot or hand has been described as not unlike the erythromelia of thrombo-angiitis obliterans, or a livid tint may predominate. The pulsation in the affected vessel or beyond the site of obstruction disappears. Sensory disturbances have been reported, such as hyperesthesia, and anaesthesia. Ischemia is not infrequent, and may possibly be elicited on elevation of the extremity.

Improvement in symptoms may occur spontaneously or after treatment. Without treatment, however, the condition gradually becomes worse and gangrene may appear after months or lapse of years. The gangrene is usually sudden in its appearance and progressive. With it pain becomes excruciating. In most cases a patch of dry gangrene appears in the neighborhood of a toe. Usually this gangrene is limited to one or more toes, but may extend for a variable distance.

Some of the French authors describe a special form with intermittent claudication, although careful anamnestic data would probably reveal that this symptom is common to many of the cases. Crises of intermittent claudication with exceptional pallor of the extremities also occur.

The affected arteries may be tender to touch, their pulsations reduced. With the more rapid development of lesions, with or without thrombosis, there may develop sudden pain in the calf of the leg followed by paresthesia and numbness. The pain is aggravated by motion, often increased at night. At the same time the extremity becomes colder and pale, and the symptoms may gradually abate. Or, the symptoms may give way to those of impending or of well developed gangrene.

Clinical Forms.—A survey of the literature permits of the following grouping of cases, which, however, must not be accepted as having any further value than for purposes of clinical orientation.

First, syphilitic arteritis of the lower extremities with clinical picture of intermittent claudication.

Second, simultaneous clinical involvement of the arteries of the upper and lower extremities.

Third, associated lesions of the intestinal arteries.

Fourth, lesions of all the vessels of the lower extremities.

Fifth, lesions of the digital arteries alone with benign course (gangrene of digits).

A clinical grouping given by other authors includes a subacute and an acute variety.

1. *The Slow or Progressive Form*.—The symptoms may or may not be accompanied by intermittent claudication (Druelle).

(a) *Without Intermittent Claudication*.—The first symptom that directs the attention of the patient to the arterial affection is pain of variable intensity along the course of one of the known arteries of the limb. This develops slowly and is aggravated by pressure and movement of the affected extremity. The artery may be converted into a tender and hard cord. The respective pulsations are diminished, and the circulation may be impaired in the distal parts, the skin being pale, cold, or even livid. With treatment, however, and rest, the circulation may be restored, but recurrences are possible. Of the other sensory disturbances, there may be formication and other paresthesiae, or even anaesthesia. Later disturbances in motility and even contractures may supervene; trophic disturbances are also reported. After administration of mercury all of these symptoms may diminish and even disappear.

If treatment is not instituted, gangrene may result. This is usually of the dry type, may be limited to the toes or the fingers, but may involve the larger part of an extremity.

(b) *Cases with Intermittent Claudication*.—It is not quite clear why some of the authors emphasize the occurrence of this as a separate form; for it has been shown that this complex may obtain in all the varieties of obstructive arterial affection of the extremities. Possibly its significance has been emphasized because it may be a prominent feature in young individuals previously healthy, when attacked with syphilitic lesions of the vessels.

2. *Acute Form*.—The most characteristic symptom is pain, which is often intense, indeed, so excruciating that the patient constantly seeks to alter the position of the limb in the hope of obtaining relief. Some even pray for amputation because of their suffering.¹ Other severe symptoms are associated. The limb may become cold, have a cadaveric appearance, and even the sensations of certain parts of the limb may become abolished. In this acute form the French authors speak of *painful anesthesia*, which means an association of pain and an anesthesia of the part. With it the motile functions are in abeyance. The skin may become livid and mortification may set in.

Examination reveals the disappearance of the pedal pulses, posterior tibial, popliteal and even the femoral. In these types the gangrene may be more extensive than in the slow forms, and when it begins in the toes, may rapidly extend so as to invade a large part of the leg.

3. *A recurring form* of gangrene due to syphilitic arteritis is reported. In its clinical course this closely resembles that of thrombo-angiitis obliterans.

4. *Syphilitic Arteritis in Advanced Age*.—Patients, who by reason of their age, may be expected to present arteriosclerotic changes may, when lues is present, present a pathological and clinical picture hard to interpret from the etiologic standpoint.

¹ Compare with similar cases of acute thrombo-angiitis (Chap. XLI).

CHAPTER LXXIX

PERIARTERITIS NODOSA

This is a rather rare disease (about 52 cases reported in the literature), and was first described by Kussmaul and Maier.¹ The characteristic lesion is an exudative inflammation of the periadventitial structures, the adventitia, the media, and sometimes the intima. By virtue of necrosis of the media, both true and false aneurysms with thrombosis (sometimes with hemorrhagic



FIG. 153.—Periarteritis nodosa. *a*, Thrombus containing leucocytes in the lumen; *b*, internal elastica interrupted through inflammatory process; *c*, media; *d*, fresh process of degeneration; *e*, large focus of degeneration; *f*, inflammatory infiltration of media; *g*, external elastic coat with numerous interruptions; *h*, adventitia with leucocytic infiltration. (*Benda*)

extravasation) may develop. These lesions usually effect varying degrees of injuries to the area supplied by the arteries, such as infarction and coagulation necrosis. Later, proliferative adventitial or intimal changes, reparative or organization processes may take place. The name was given because of the presence of so-called nodules formed by multiple thrombosed aneurysms often arising from vessels of small size.

The important lesions in this disease are the necroses and the hemorrhages of the media, the inflammatory (leucocytic) infiltrations of all three layers with the associated thromboses in the lumen (Fig 153), and the aneurysms, which alterations may occur in numerous discrete foci. The lesions tend to healing with connective tissue cicatrization of the mural changes, with proliferation of the intima and resulting obliterating endarteritis; or, with organization of thrombi (Fig 154).

¹ Kussmaul and Maier, *Deutsch. Arch. f. klin. Med.*, 1366, I, 484.

Clinical Manifestations.—Depending upon the seat of the arterial lesion, cardiac, pulmonary, renal, intestinal, cerebral, abdominal, and manifestations in the extremities, are the chief features of the symptomatology. Detailed accounts will be found in articles by Lamb¹ and Klotz.² Here we are concerned only with those data that the literature offers as referable to involvement of the arteries of the extremities.

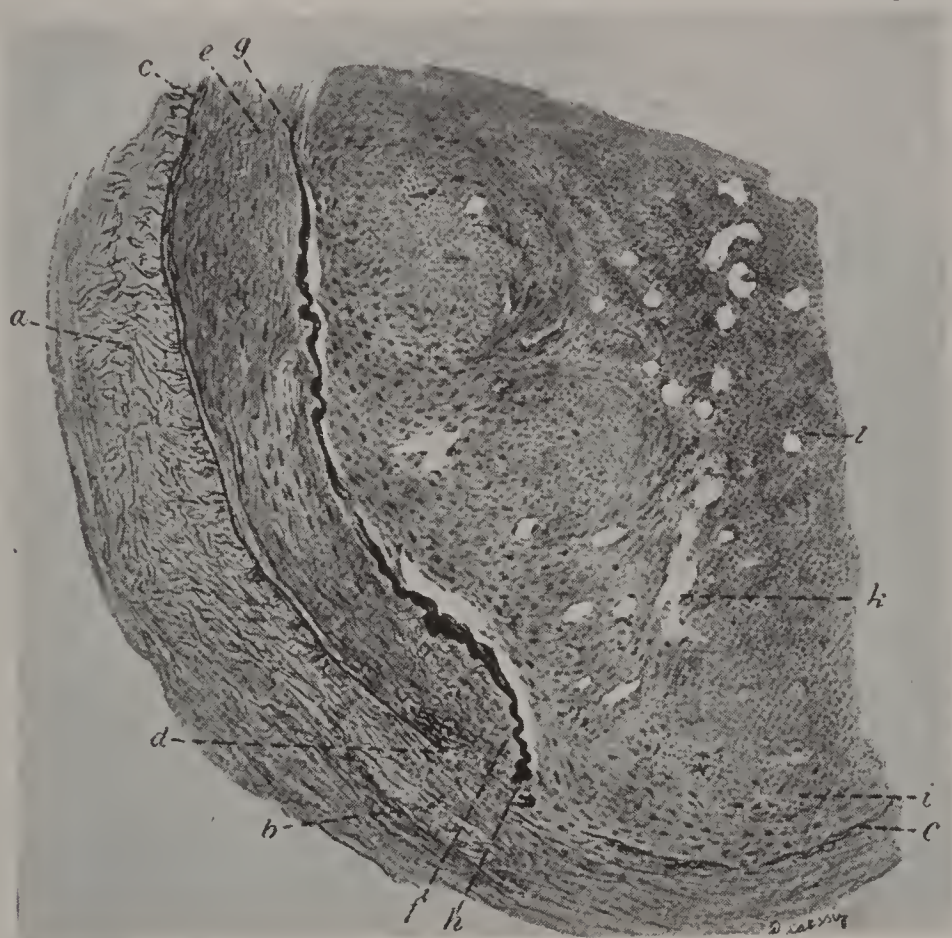


FIG. 154.—Periarteritis nodosa in a branch of the superior mesenteric artery with recent organization of thrombus. *a*, Adventitia; *b*, cicatrization of inflammatory focus; *c*, external elastic lamina; at *d*, interruption of the elastica by cicatricial tissue; *e*, media; at *f*, interruption by cicatricial tissue; *g*, internal elastic lamina; at *h*, the latter is interrupted; *i*, granulation tissue in the intima with new vessels (*k*); *l*, mass of thrombosis. (*Benda*)

Manifestations in Extremities.—Pain and cramp-like sensations have been described. Where the subcutaneous vessels have shown specific pathological changes, pain and nodule formation in the areas involved have been demonstrated. When the latter are present, extirpation of a nodule and pathological examination may lead to correct diagnosis.

Pains in the voluntary muscles and along the peripheral nerves are a feature and may be so pronounced as to be diagnosticated as neuritis, poliomyositis or trichinosis.

¹ Lamb, Arch. Int. Med., 1914, 14, 481.

² Klotz, Jour. Med. Res., 1917, 37, No. 1, p. 1.

CHAPTER LXXX

SYPHILITIC DISEASE OF THE VEINS

Only those lesions will be described here that may give a picture of migrating phlebitis that could be mistaken for similar phenomena in thrombo-angiitis obliterans.

The lesions of syphilitic phlebitis should be recognized and differentiated from other forms especially from thrombo-angiitis obliterans. Indeed, certain histologic similarities may require the following exposition for clarification.

Clinical Characteristics.—The veins of the extremities, particularly those of the lower extremities, are usually affected. In rare cases, phlebitis has been observed in the face. Frieboes¹ has reported 2 such cases. In 1 of these, there appeared during the secondary stage, bilateral cord-like indurated areas $1\frac{1}{2}$ to 2 cm. in length, and of the thickness of a lead pencil. These were situated in the temporal region just adjacent to the eye, causing some slight prominence of the overlying skin. Under antisymphilitic therapy these disappeared. In a second case, similar cord-like manifestations appeared along the course of the vessel, just under the skin in both temporal regions, due to inflammatory processes in the veins.

According to some authors the veins may be involved so gradually that careful palpation is necessary to elicit pain along the venous cords. However, the attention of the patient may be drawn to the part by a sensation of discomfort, a tenderness of the affected limb, or, muscular cramps at night, and formication.

The seat of the phlebitis is usually one of the superficial veins of the extremities, such as the internal saphenous. On inspection one finds the affected limb normal in volume, with sometimes a slight rosy discoloration of the overlying skin, the discolored area has about the width of one finger. The venous cord is indurated, varying in size from a quill to a lead pencil, usually not adherent to the skin at first. Three varieties have been described: first, partial, syphilitic phlebitis; second, segmentary; and third, total. This grouping depends upon whether the lesion is limited to a portion of the vein, its course over a segment of the limb, or its total length. Sometimes slight edema is present in the region of the involved vein.

The clinical course is a rapid onset with inflammatory symptoms, then a gradual decline, leaving an indurated cord under the skin. All manifestations disappear within 4–6 weeks. Embolism is very rare in the course of syphilitic phlebitis. In some cases recurrences have been observed, various veins being successively involved.

When the deep veins are involved the clinical picture may be that of milk-leg, but both veins of the upper and lower extremities may be affected. It is rare for but one vein to be involved, a multiplicity of venous lesions being the rule.

Pathology.—Descriptions of the histologic changes vary greatly in the literature. The striking pictures observed by some are produced by the presence of foci containing giant cells and nodules in the perivascular tissue, suggestive of miliary tubercles. According to other authors, such lesions

¹ Frieboes, *Dermat. Ztschr.*, 1913, **20**, 125.

have not been seen, and the alterations are confined to the vessel itself with the production of a clot without any recognizable, specific, architectural changes. It would seem, therefore, that for differentiation from thromboangiitis obliterans only those observations in which giant cells are a feature need special mention.

In most cases red thrombosis was observable, the lumen being more or less completely filled with a clot. According to Roques the intima is altered, being replaced by tissue made up of round cells, fusiform cells, and a deposition of connective tissue. This new formed tissue produces thickening of varying degrees.

The internal elastica is well preserved, a solution of continuity being present only in a few places.

The other coats contain a large number of cells of variable shape, some round, others fusiform or elongated. Giant cells were absent.

Spirochætae pallida have been demonstrated in the vein walls by Ravaut and Ponselle.¹

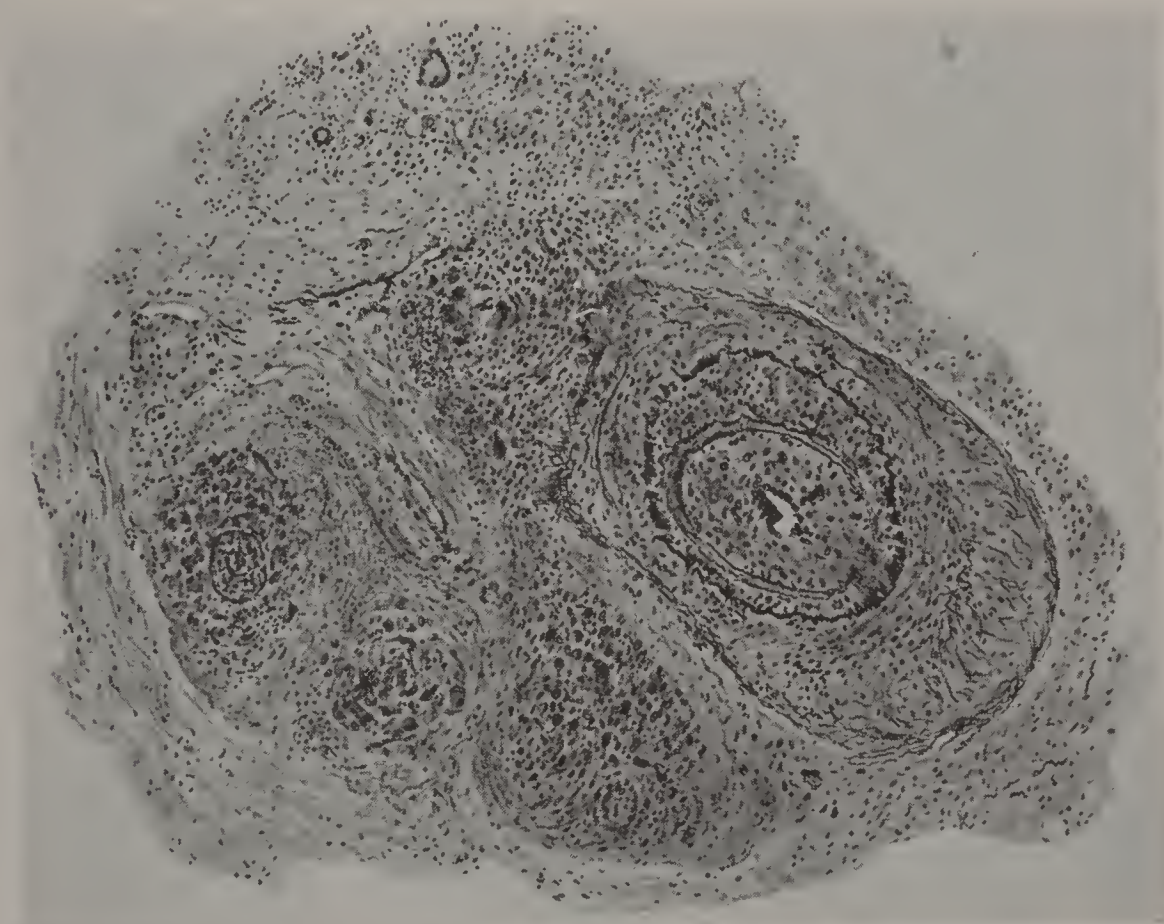


FIG. 155.—Syphilitic lesions of the vessels and perivascular tissue in phlebitic nodule removed from veins; obliterating proliferative lesion seen in larger vein on the right; on the left, a small vein is infiltrated, its elastica conserved; below and above, syphilitic miliary tubercle-like nodules with giant cells. (Frieboes)

Specimens were extirpated by Frieboes and the lesions found may be described as (1) of the perivascular tissues, and (2) of the vessels themselves.

A characteristic and distinguishing feature contrasted with thromboangiitis obliterans, is the inflammatory lesion outside of the vascular domain. These lesions have been variously described, but the presence of giant cells of the Langhans type associated with endothelioid plasma and mononuclear cells makes a picture that is not found in the extravascular tissues in thromboangiitis obliterans. Frieboes describes an inflammatory lesion composed of an infiltrate of epithelioid, mononuclear, and plasma cells, associated

¹ Ravaut and Ponselle, Soc. Med. des Hôpitaux, Jan. 12, 1906.

with destructive lesions of the connective tissue fibers and degeneration of capillaries. There are also foci or conglomerates of such cells and occasional giant cells of the Langhans type. Some of the nodules in the connective tissue composed of endothelioid, mononuclear and giant cells are suggestive of tuberculosis.

The smaller vessels in the connective tissue show an arteritis obliterans with degeneration of the whole vessel by reason of reactive processes. There is an intense proliferation of the intima of the small vessels, almost occluding their lumina.

In the larger veins the media is infiltrated with cells, the elastic fibers being displaced and spread apart and fragmented. With this change, the lumen of the vessel becomes eccentrically displaced. The process is one of vascular destruction by reason of new formed inflammatory tissue. The proliferating cells constituting the latter replace the vascular wall, so that in places nothing but a few elastic fibers remain, as shadows of the inflamed vessel; or, a few concentrically placed cellular groups within elastic fibers may be the only remnant of a vessel (destructive lesion).

In another case the infiltrate was found especially confined to the neighborhood of the vessels, occasional giant cells being interspersed here and there, amongst the new formed perivascular elements.

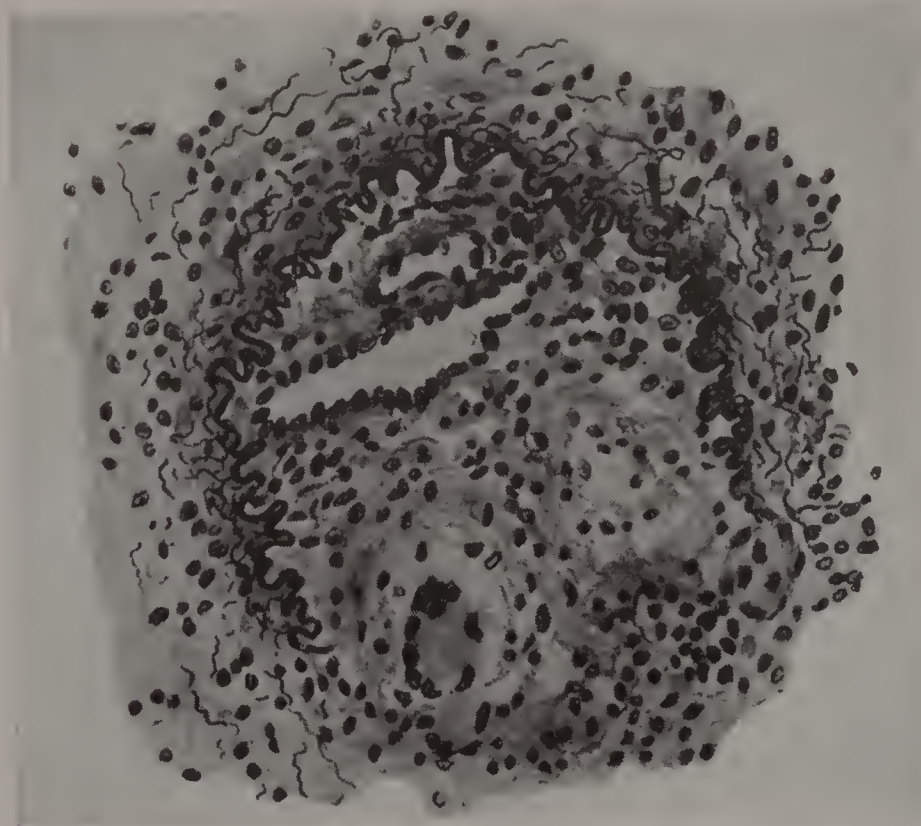


FIG. 156.—Destructive inflammatory lesion of syphilitic nature in a vein. The elastica is destroyed; below, the lumen of the vessel is occupied by new formed vessels, giant cells, endothelioid and plasma cells. (*Frieboes*)

The vascular changes in the second case of Frieboes showed all transitions from early endothelioid proliferation within the vessel, up to *complete destruction*.

In Fig. 155 the wall is seen infiltrated with cells causing encroachment upon the lumen and remarkable enlargement of the total diameter of the vascular section. The elastic fibers are separated, split, torn and displaced. On the left in the picture there is a small vein in which the elastic ring is still conserved, but the lumen is filled with proliferating endothelium. Below in the picture there are nodules composed of proliferating cells and giant cells. These are the foci suggestive of miliary tubercles.

Fig. 156 shows clearly the destruction of the elastic ring, and the lumen contains endothelioid cells, mononuclear and giant cells and new formed vessels.

In short, the aforementioned lesions differ from those of thrombo-angiitis obliterans, in that foci of syphilitic inflammatory lesions are present in the tissues outside of the vessels; secondly, in that they are of exquisitely productive nature with a tendency to cause destruction of the vessels. This is accomplished through the action on the elastic and connective tissue elements; and finally, complete obliteration of the lumen by new formed tissue with or without thrombosis may be the significant intravascular lesion.

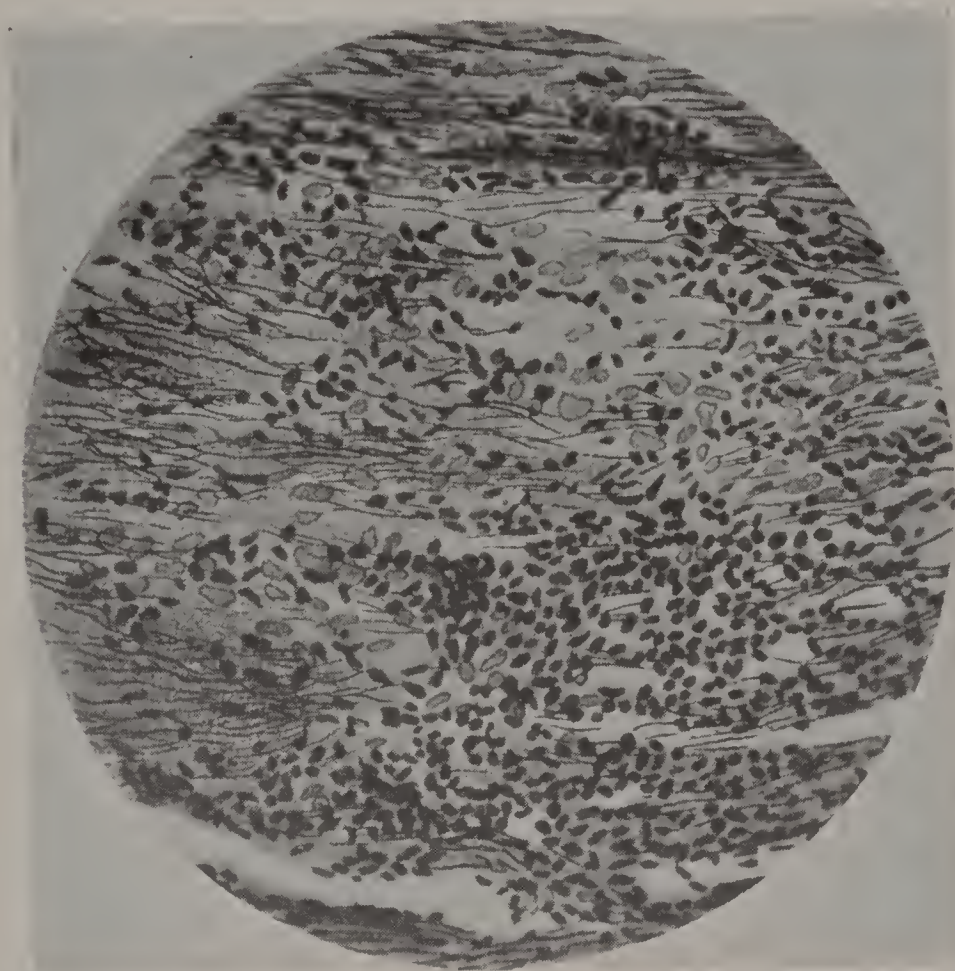


FIG. 157.—Inflammatory infiltration in the media of a vein in secondary syphilis. The cells are mostly of the plasma cell type with some endothelioid proliferation and round cell infiltration. (Hofmann)

The inflammatory changes in the veins vary according to the literature. Those described by Hofmann¹ resemble those of thrombo-angiitis obliterans so closely that the points of differentiation are worthy of note. There are enough differences in the histologic picture of the two lesions to enable the microscopist to make a distinction.

A thrombotic and inflammatory lesion is present in the veins (Hofmann). The presence of giant cells we believe might lead to confusion in differentiation from lesions of thrombo-angiitis obliterans.

The inflammatory infiltration of the wall of the vessel differs from that of thrombo-angiitis obliterans in that the predominating cells are plasma cells, particularly grouped about the vasa vasorum. Besides this, the media is the seat of marked proliferation of the fixed cells, and of round-cell collections (Fig. 157). Just under the elastica interna there is an intensive inflamma-

¹ Hofmann, Arch. f. Dermat. u. Syph., 1905, 73, p. 245.

tory lesion represented by proliferation of endothelioid cells, fixed connective tissue cells, collections of plasma cells, together with occasional giant cells.

This localization (within the vessel wall) together with the presence of giant cells in this layer (Fig. 158) is characteristic of the syphilitic lesion. The internal elastic membrane is rarefied, displaced and destroyed in places.

The intima shows extensive proliferation of cells of varying degrees, being thicker in some places than in others. Parietal thrombi are said to originate at points where the lesions are most intensive.

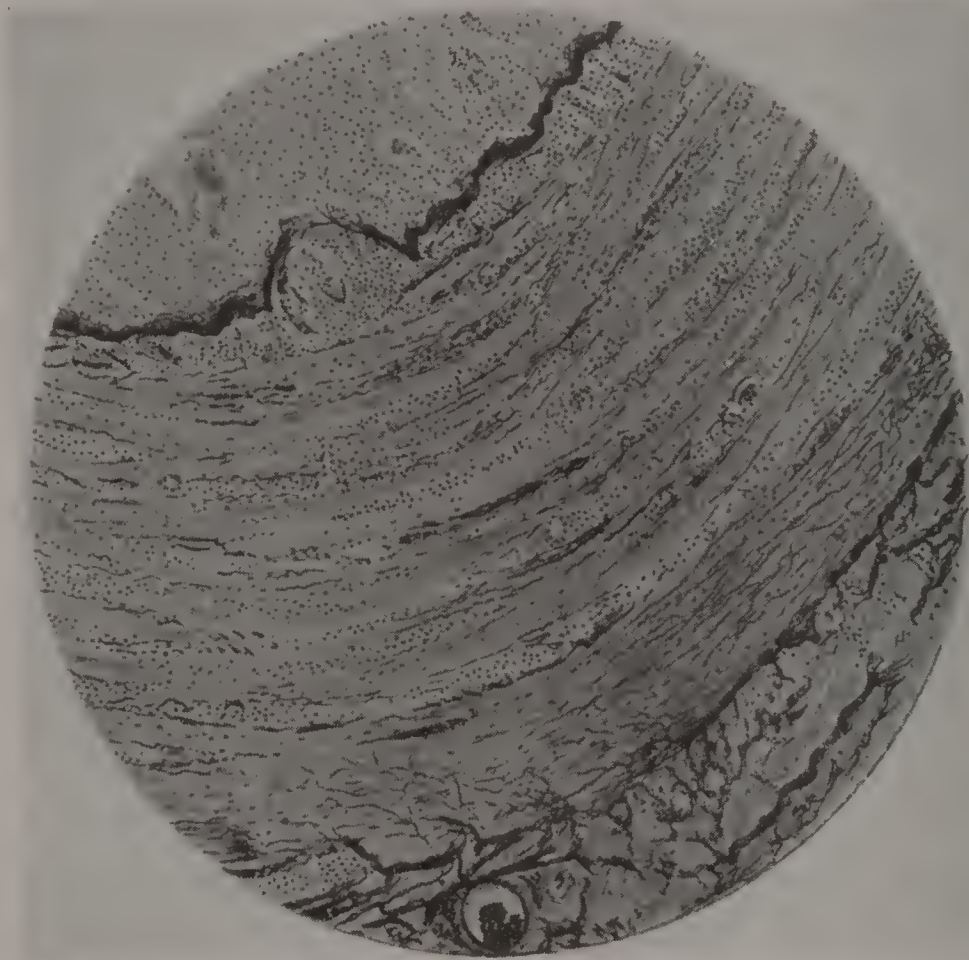


FIG. 158.—Syphilitic lesion in vein showing giant cells in clot, and giant cells in foci under the internal elastic coat. (Hofmann)

The thrombus contains large numbers of giant cells of the Langhans type. In the periphery of the clot, the connective tissue fibers are developed, but the greater part of the thrombus is made up of red blood cells and blood platelets with considerable fibrin.

Tertiary or Late Form.—The studies of Roques have shown that the deep veins of the upper extremity, the popliteal and posterior tibial may be involved. In the late stage of syphilis the multiplicity of lesions is not observed, and the affection seems to be less severe and more diffuse.

The affected limb is painful and heavy, and becomes rapidly useless from the functional standpoint, by reason of augmentation in volume. With this there may be a slight elevation of temperature.

The enlargement of the limb is striking due to edema, which may involve the whole of the extremity. The limb feels hard. When the edema is distributed about the vein, an elongated area of tumefaction is developed which corresponds to the course of the vessel.

Sensory and trophic disturbances are not associated. The progress of the phlebitis is slow and yields to antisiphilitic treatment, the symptoms

disappearing *in toto* in from 6–8 weeks after treatment has been instituted. Recurrences have not been observed.

Histo-pathology of Tertiary Phlebitis.—The lumen of the popliteal vein in one case (Roques¹) was filled with a clot already in a state of partial organization. The intima was markedly thickened, containing small rounded cells, and fusiform cells with new formed connective tissue.

The other coats, the media and adventitia, contained an abundance of alien cells. These are regarded by this author as representing an infiltration with young connective tissue.

Diagnosis of Syphilitic Phlebitis.—An indurated cord corresponding to the anatomical course of a superficial vein in a syphilitic when of recent origin must be regarded as possibly of luetic origin. The onset, however, is slow and insidious, and a number of veins may be affected simultaneously or consecutively. This type must be distinguished from a number of others, from thrombo-angiitis obliterans, phlebitis of rheumatism, erythema nodosum, nodular lymphangitis, syphilitic myositis and syphilitic gumma in a vein.

Rheumatismal Phlebitis.—According to the French authors phlebitis of rheumatism is accompanied by recrudescence and exaggeration of the febrile phenomena and of the pain. As a rule polyarthritides is associated, or cardiac, pericardiac, or pleuritic lesions. The presence of syphilitic stigmata are of the utmost value in diagnosis.

Erythema nodosum is easily distinguished since in a case of phlebitis the relation to the vein, the mobility, the absence of adherence to the skin and the redness of erythema nodosum are characteristic.

Thrombo-angiitis Obliterans.—In this disease the nodules are of two types, the nodules, and the cord-like swellings. In both there is marked tenderness, adhesion to the skin, and depending upon the situation and extent of the lesion, the vein is also adherent to the deeper parts. In addition, there are usually associated the evidences of obliteration of the deep vessels. Biopsy of excised veins permits of microscopic differentiation.

Syphilitic Gumma (Tertiary).—Here the skin and deeper parts are also involved. In the *nodular lymphangitides* the redness is striking and the involvement of the regional lymph node is regularly present.

In syphilitic myositis there are also hard nodosities, somewhat elongated, but these can be demonstrated to lie in muscle, and are much deeper than the inflammatory lesions in the veins.

In syphilitic gumma of the veins a veritable tumor is developed, that rather suggests a neoplasm or tuberculoma than thrombo-phlebitis.

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CHAPTER LXXXI

MIGRATING PHLEBITIS—MISCELLANEOUS VARIETIES

Whilst the phlebitis of subcutaneous veins is regularly attended with obturating thrombosis in thrombo-angiitis obliterans and in syphilis, other non-thrombotic varieties have been described.

Phlebitis Migrans with Pulmonary Tuberculosis.—The following clinical and pathological picture is given by Schwarz. The affection involves superficial veins acutely with signs of inflammatory swelling, tenderness and redness of the overlying integument. An inflammatory process takes place in the vessel wall with edema and leukocytic infiltration of media and adventitia. This is followed by the formation of new connective tissue and new vessels, but *no thrombosis* occurs.

In short, in advanced tuberculous individuals circumscribed painful, inflammatory foci are found in superficial veins, the latter conserving their permeability. Fusiform swellings occur implicating the overlying skin. The acute lesions in the veins gradually give way to chronic fibrotic thickening, the final product being unknown since no material in this stage has been studied pathologically.

Other Varieties.—There are a number of different varieties of migrating phlebitis usually involving the territory of the internal and external saphenous, the pathogenesis of which is not clear. Microscopic examination, however, of pieces excised for histological researches has demonstrated, in the author's experience, that the typical lesions of thrombo-angiitis obliterans are absent. We shall describe some of the cases that have come to our notice, giving clinical and pathological data.

1. *Focal Migrating Phlebitis of Unknown Origin.*—In some of these a history of excessive smoking over many years can be obtained. In others, however, there are no anamnestic data that throw light upon the etiology. In one such case the tributaries of the saphenous were excised, and bland thrombi demonstrated. The media was most involved in the inflammatory process, the muscular fibers being separated by migrating polynuclear leukocytes. In some sections, foci of migrating polynuclear cells and fibrin were seen to penetrate the media and enter the lumen through the intima. The accumulation of leukocytes was most intense in this zone, although also present throughout the rest of the vein wall.

C. J. R. (April 1, 1922), 33 years of age, American, had trouble in the left foot and leg for 8 months. This was described by the patient as a pain traveling from one place to another, since he did not himself detect the local changes in veins that were gradually taking place.

On examination of the left leg there were several inflamed and obliterated regions in the course of the internal saphenous, some along the inner side of the knee and leg, others along the inner border of the foot, and another inflamed cord over the lower third of the thigh. A portion of vein about $\frac{3}{4}$ of an inch in length in a situation in which the vein seemed rather acutely inflamed was excised.

Microscopic Examination.—Lesions of thrombo phlebitis with red thrombus completely occluding the vein are here found, the early organization being of the bland type. There is an inflammatory infiltration of the vein. The fibers of the media are separated by round and migrating cells and edema. The inflammatory exudate does not equally involve the walls in annular fashion, but seems to be most pronounced over certain portions of the vessel wall (Fig. 159). In some sections this focal distribution of the inflammatory process

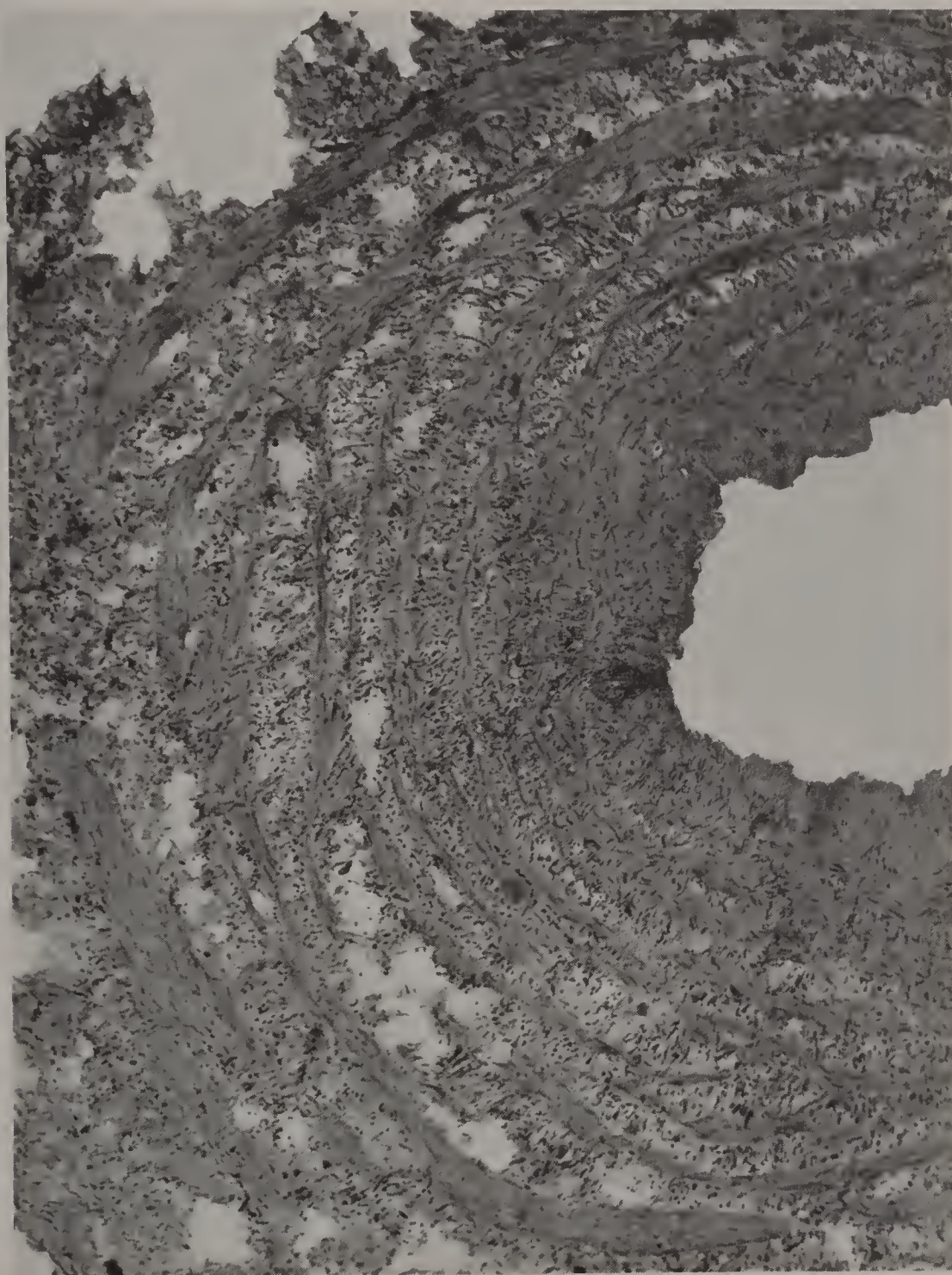


FIG. 159.—Acute phlebitis, a portion of one of the tributaries of the internal saphenous vein acutely inflamed (migrating phlebitis) in a process of unknown origin (not thrombo-angiitis obliterans); diffuse leucocytic infiltration of the muscular coat and a focus of migrating cells located at one point where the black area is seen penetrating the intima.

shows itself not only in the limitation of the inflammatory product to a portion of the wall, but also in a distinct streak-like invasion of the intima with migrating cells, in direction perpendicular to the circular fibers, as if a penetration of the intima and clot was thereby intended. In certain places intensive infiltration of the subintimal layers with inflammatory cells can be seen extending in a longitudinal direction for a variable distance (Fig. 160), another evidence of the focal distribution of the lesion. A similar inflammatory lesion can be traced for a variable distance into the tissues about the vein.

2. *Migrating Phlebitis with Infections (Non-suppurating)*.—Rheumatic phlebitis with general manifestations is referred to in Chap. LXXVI.

3. *Extensive Recurring Phlebitis*.—We occasionally encounter slowly progressive and recurring attacks of migrating thrombophlebitis over the territory of the internal saphenous vein and many of its tributaries, that may eventually lead to venous occlusion from the foot up to the cribriform opening in the femoral fascia, and possibly even into the femoral vein. The few

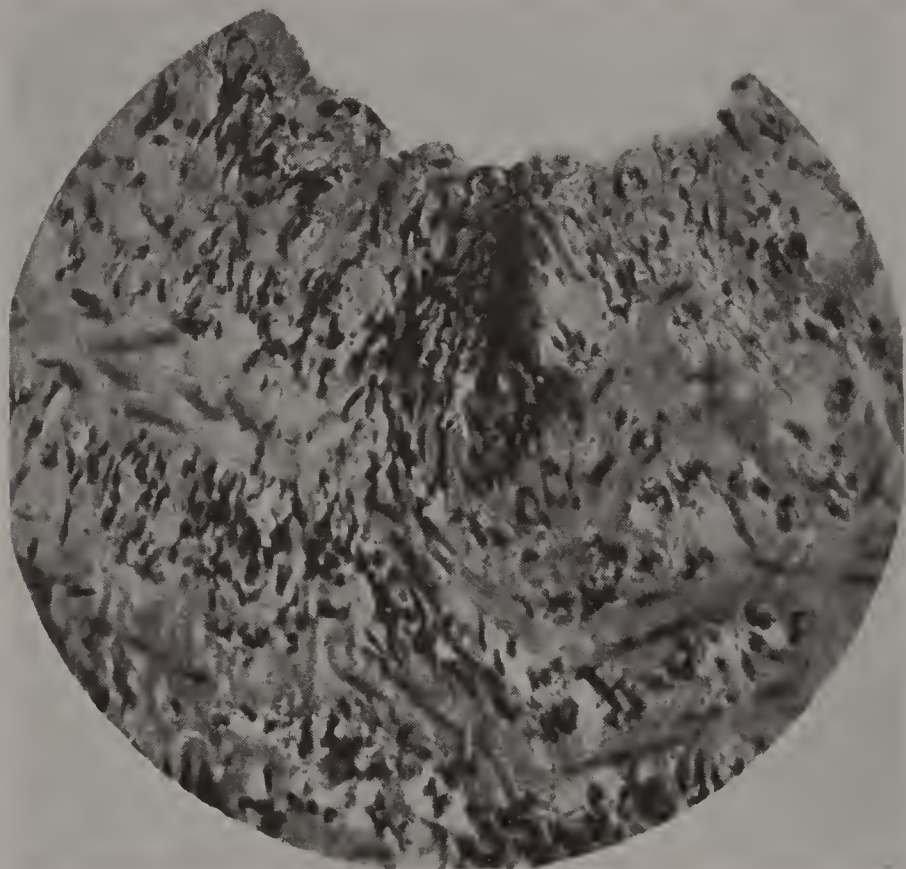


FIG. 160.—Inflammatory focus, wandering cells, leucocytes in the wall of a superficial vein; above in the region of the intima a focus of intensive migration; throughout the main wall infiltration with polynuclear leucocytes. (High power of Fig. 159)

cases observed by the author—in which thrombo-angiitis obliterans and lues could be excluded—were males, in one of whom a history of excessive smoking could be elicited. The insidious nature, the lack of exquisite tenderness and redness so characteristic of thrombo-angiitis obliterans, distinguish this form as being less intensively inflammatory. The exact etiology is unknown.

4. *Migrating phlebitis* of unknown cause possibly belonging to group (1) has been observed in young men in whom the malady was so limited in extent and so devoid of marked discomfort that material for exsection and study was refused by the patient. One case—a physician—interpreted his affection as of metabolic origin, from the observation that after some recurrences it was arrested completely by strict dietary régime.

CHAPTER LXXXII

VASCULAR OCCLUSION OF DOUBTFUL ORIGIN

It is not always possible to fathom the exact nature of the processes that may obliterate the arteries of the lower extremities. In our experience four different types of cases have presented themselves in which all of the arteries

of this territory are pulseless. In two of these the diagnosis of thrombo-angiitis obliterans can be made with a fair degree of probability; in the others no positive conclusions as to the variety of essential lesions can be arrived at. Succinctly stated, these forms are:

(1) Typical thrombo-angiitis obliterans of one lower extremity with absence of all the usual pulsations of the other, symptoms in the latter being almost nil.

(2) Absence of all the usual pulsations of one lower extremity with a history suggesting an old thrombo-angiitis.

(3) Absence of femoral and popliteal pulsations in cases in which wounds of the leg fail to heal, eventually necessitating amputation.

(4) Absence of all the pulses of *both* lower extremities, without trophic disorders, and of unknown causation.

1. We have referred elsewhere to those rare but interesting cases in which the diagnosis of the disease as it affects the vessels of one limb is clearly thrombo-angiitis obliterans, but the patient may be unaware of a similar process on the other side. This is due to the absence or paucity of subjective symptoms, but on investigation all the pulses will be found absent.

2. Here enough anamnestic data can be elicited to warrant the belief that some time in the past evidences of an active or even "acute" thrombo-angiitis obliterans have been present in the limb under consideration.

3. Not uncommonly will we encounter cases in which there is a history of a long state of invalidism. This is often attributed to a minor injury, accidental or unwittingly self-inflicted, beginning in a toe or somewhere in the leg, or even initiated by a minor apparently inconsequential operation done by a surgeon for a trifling disorder. The wound thus occasioned fails to heal, chronic ulceration ensues and then the patient is confined to the house for weeks or months. Eventually a "conservative" amputation is resorted to somewhere through the leg, and even this wound does not heal. Cases have come to the author's notice where the stump did finally close below the knee and in others ablation higher up had been eventually found necessary.

In such patients the obliteration of all of the palpable arteries was the fundamental cause of the local nutritional failure. One could demonstrate the absence of the external iliac, femoral and popliteal pulsations. Since all instances of this type so far observed, have had some part of the extremity removed, the interpretation of the exact nature of the vascular lesions is difficult. The absence of intermittent claudication, previous trophic disorders, pain, coldness and blueness—in short, all of the usual signs of deranged circulation, and the latency of the affection until the infliction of the initiating wound—all this puts the affection into a doubtful category, one admitting of multiple causal interpretation.

Thus, we may assume that any of the following pathological processes without clinical manifestations may account for the vascular blockage: (1) Luetic arterial disease; (2) atherosclerosis with insidious thrombosis; (3) thrombo-angiitis obliterans without symptoms; (4) bland thrombosis of the small peripheral vessels with ascending accretion clots (mechanical); (5) embolic closure without symptoms; or finally, (6) an inflammatory lesion (arteritis) with thrombotic obliteration of unknown variety and origin.

If we analyze these possibilities, only the first, fourth, fifth, and sixth are at all likely in view of the facts and data elsewhere adduced.

4. We shall give by way of illustration of this variety an instructive history of a patient in whom inability to walk and pain in both lower extremities from the hip down were the significant symptoms that led to the discovery

of the ubiquitous absence of the pulses. Whether we were dealing here with the result of a succession of latent embolism and thrombosis, or some other lesion, we are at a loss to decide.

G. G., physician, American, 43 years of age, gave the following history November 16, 1921. The malady commenced suddenly in June, 1919, with symptoms suggesting angina or pulmonary embolism, the physician in charge stating that there was cyanosis of the neck and face at the onset, with rapid pulse and threatening collapse. Following this the patient was very ill for 10 days, with temperature ranging from 100° to 101°, with a rapid pulse, but with no symptoms referable to the lower extremities.

In April, 1921, his legs suddenly gave way after a slight exertion because of sudden pain in both hips radiating down the legs, so that he was unable to walk. He rapidly recovered from this, but ever since then the pain on exertion and the weakness in both lower extremities have persisted; leukocyte count 22,000.

November, 1921, complete status (Dr. L. Barker) revealed nothing sufficiently significant in explanation of the findings of vascular occlusion.

Physical examination made by the author November, 1921, demonstrated absence of pulsation in both femorals and accessible portions of the external iliacs, the popliteal, posterior tibial and dorsalis pedis arteries. On elevation of the limbs there is very slight ischemia, and there is but a suggestion of rubor on allowing the legs to hang down; trophic disorders are absent; 17,300 leukocytes.

In June, 1922, the patient stated that the pain in the lower extremities had diminished in intensity; that he had had one attack of cardiac pain which left a pericardiac sound and systolic murmur, and that the leukocytic count had varied from 14,000 to 18,000 since last November.

In September, 1922, the patient further stated that he had had no pain in the extremities when at rest, but cramp-like pain on walking. On elevation of both extremities there is a moderate ischemia, but the color is retained in the dependent position; slight cyanosis of both feet, more marked in the left; both feet colder than normal; absence of all pulsations in both extremities from the femoral artery down.

Epicrisis.—In the diagnostic interpretation of imperceptible pulses over so extensive a territory, it must be remembered that absent arterial beat is not exactly equivalent to occlusion. Perhaps, in cases of this sort, some arteries in which the pulse is extinct are still patent, and allow a small amount of blood to permeate, the occlusion being higher up. This assumption is a warrantable one, for it is based on the pathological findings in other cases in which a return of pulse in the radial artery occurred after embolic closure (Chap. LXXXV, p. 495).

If this view is correct, an explanation is at hand for the meager symptomatology in cases of this sort.

CHAPTER LXXXIII

MAL PERFORANT

Our first knowledge of this disease dates back to the year 1852, when Nélaton¹ described an affection characterized by an indolent ulcer of the foot. This complication, although descriptive of a case of lepra, gave impetus to the study of what since has become known as *mal perforant*, *malum perforans pedis*, or *mal plantaire perforant* of Vésigné.²

For a correct conception of this symptom-complex—it cannot be correctly considered as a unity or separate malady—we must accept and comprehend

¹ Nélaton, Gaz. d. hôp., Jan. 10, 1852.

² Vésigné, Gaz. d. hôp., Feb. 5, 1852.

that not only may the clinical picture vary, but also that the manifestations may be brought about by wholly and widely varied causes. Here we are confronted with a situation similar to that described under Intermittent Claudication (Chap. XXVI) and should more correctly view Perforating Ulcer of the foot as brought about by widely different causal factors. The literature, however, is so complete and comprehensive, and so many authors of note have described the condition under this name (*malum perforans pedis*), that it may be well to adhere to the nomenclature, calling attention to the advisability of investigating every case for the discovery of the underlying malady.

Although the importance of diseased arteries has been minimized in this connection by a number of authors, it must be strongly emphasized that trophic lesions of this type may result from both obstructive arterial and neurogenic causes.

Etiology.—The condition is most frequently observed in males, particularly over the age of forty. The laboring and menial classes seem to be most frequently affected. The site of predilection corresponds with the point of pressure on standing and walking. Thus, the plantar surface of the foot, the metatarso-phalangeal joint, especially over the borders of the first and fifth toes, over the heel, and more rarely in the sole, are the most frequent sites. It is usually unilateral, but may occur simultaneously in both feet. The weight of opinion favors the view that a variety of fundamental affections may produce the same clinical picture.

Several theories regarding etiology have been suggested: first, the mechanical theory; second, the vascular; third, the nervous and neurogenic theories; and fourth the arthropathic and osteopathic theories.

The Mechanical Theory.—Pressure and trauma should be considered merely as contributory factors in determining the site of development of an ulcer, and not as the underlying cause. In view of the fact that perforating ulcers can occur in situations that are not under the influence of mechanical injury, pressure or trauma, and seem to heal with the patient in bed at complete rest, the mechanical theory has justly lost support.

The Vascular Theory.—Although certain authors (Hofmann¹) conclude from a study of the literature that obliteration of the arteries plays but a subsidiary rôle, the author is of the opinion that occluded arteries whether due to arteriosclerosis, thrombosis, or thrombo-angiitis obliterans may some time be followed by the development of perforating ulcers, clinically indistinguishable from those of less evident organic cause. Levai² and others are sponsors for the vascular theory. A careful investigation of the condition of the vessels of the lower extremities, including the femoral, the popliteal, the dorsalis pedis and posterior tibial arteries, and a search for the typical objective manifestations of arterial disease, would often reveal a causal relationship between the vascular obturation and the trophic symptoms.

The Nervous or Neurogenic Theory.—A number of different diseases of the nervous system may be attended with sensory or vasomotor paralyses or palsies in the territory of the lower extremities, and in consequence be associated with the appearance of trophic ulcers, of which the so-called *mal perforant* is a prominent and frequent example. Mal perforant may even be a symptom of either *peripheral* or *central* nerve lesion.

Peripheral Nerve Lesions.—The nerve lesions may be limited to the territory in the immediate vicinity of the ulcer, or implicate a larger part of

¹ Hofmann, *Ergebn. d. Chir. u. Orth.*, VIII, p. 909.

² Levai, *Deutsch. Ztschr. f. Chir.*, 1898, 49, 558.

the nerve distribution of the corresponding lower extremity. Peripheral neuritis as the result of freezing, burns, wounds, contusions and traumata of various kinds has been reported; so also lesions of the posterior sacral roots or injuries to the sciatic nerve, and tumors that involve the larger nerves or compress them. Other types of neuritis due to leprosy, alcoholism, lues and arteriosclerosis are also said to lead to the formation of trophic ulcers of the foot. It would appear that the anesthesia resulting from the observed lesions is in great part responsible for the formation of ulcers.

Lesions of the Central Nervous System.—These are of greater importance, particularly tabes dorsalis. Other spinal diseases may play a rôle in the



FIG. 161.—Perforating ulcers over the inner margin of the foot, second toe and outer margin of the foot. (Hofmann)

etiology, such as fractures of the vertebræ with injuries to the spinal cord, tumors of the spinal cord, spina bifida aperta, or occulta, and syringomyelia. A few cases have been described associated with progressive paralysis, progressive muscular atrophy, amyotrophic lateral sclerosis, and spastic paraplegia.

Certain constitutional diseases (diabetes) have been held responsible for *mal perforant*, but the pedal ulcer of diabetes does not usually belong in this category. The painful nature of the ulcer in diabetes is in striking contrast to the non-painful trophic disturbances associated with nervous disorders. To what extent the presence of sugar in the blood, the lesions of the peripheral cutaneous nerves, or the arteriosclerotic changes are participants in the production of trophic ulcers in diabetes is discussed elsewhere.

A peripheral localized neuritis, possibly of alcoholic origin is regarded by Hofmann¹ as the probable cause of the occurrence of mal perforant amongst the menial classes of Southern Tyrol. This author observed a large number of cases (19) in males over 40 years of age, in whom excessive alcoholism seems to be the most important etiologic factor, and was attended with evidence of diminished sensibility in the neighborhood of the perforating ulcer. Since no other cause could be found, the author attempts to explain the development of the trophic lesion on the basis of alcoholic peripheral neuritis possibly furthered by arteriosclerotic lesions.

The Bone and Joint Theory.—The development of perforating ulcer² has been attributed to primary bone and joint lesions.



FIG. 162.—Extensive destruction of the head of the fifth metatarsal bone corresponding to a callus in this region. (Hofmann)

Clinical Course and Symptoms.—At one of the sites of predilection, over the sole, the ball of the big toe (Fig. 161), the outer border of the metatarsal phalangeal joint of the big toe, or at the heel, we are wont to observe the formation of a marked callus. Although this of itself is of no diagnostic import (since it occurs in the healthy individual), the next step in the disintegration of the tissues is significant. In the center of the callus, the horny layer becomes attenuated and some secretion begins to accumulate, lifting the overlying skin away and thus producing a superficial defect. The superficial ulcer thus formed shows little or no tendency to heal, and even though healing

¹ Hofmann, *Ergebn. d. Chir. u. Orth.*, 1914, Bd. VIII, pp. 916-917.

² Levy, *Ergebn. d. Chir. u. Orth.*, Berlin, 1911, 2, 56; also *Beitr. z. klin. Chir.*, 1910, 70, H. 2 and 3.

may take place, a recurrence is the rule. As the ulcer enlarges, it also increases in depth, conserving its circular external outline, and being well demarcated by a wall of thickened epidermis. At first a thin watery or serous secretion is exuded, and putrid collections form, when secondary infection takes place. As a rule, this affliction is painless, and in most of the cases sensory disturbances with diminished sensibility can be detected in the immediate vicinity. Where the ulcer and the surrounding parts are tender and painful, certain authors would rule out true mal perforant. If this view is accepted, the perforating ulcers associated with thrombo-angiitis obliterans, diabetes, and arteriosclerosis must be excluded, and only those due to neurogenic disturbance accepted as belonging to this category.

Joint and Bone Lesions.—Authors are at variance as to the relationship of arthropathies and bony changes occurring in the immediate vicinity of perforating ulcers. There are some (Levy) who describe a primary causal relationship between the deep seated and superficial lesions, whilst there is the opposite school who contend that the bones and joints are merely secondarily involved. Perhaps the truth would more correctly be placed in a middle ground, since arthropathies may exist both independently and as a sequence of the trophic ulcers.

Not infrequently, both in the neurogenic type of mal perforant, as well as in the deep seated ulcerative lesions associated with vascular disease, destruction of bones and joints occurs (Fig. 162). This would seem to be the rule in all the advanced cases. In at least 50 per cent, if not more, of the earlier cases, the corresponding joint has been found uninvolved in the X-ray picture. Arthropathies involving a number of articulations of the foot may simultaneously occur, without necessarily being associated with correspondingly situated ulcers.

However, the X-ray is of exceedingly great value since the finding of arthropathies may call attention to the possible existence of spinal lesions. The X-ray examination will be particularly valuable when it discloses neuro-pathic joint changes without any definite evidences of nerve disease being demonstrable, but with distinct signs of local anesthesia.

Prognosis.—This depends greatly upon the underlying nerve disorder. The possible complications, such as lymphangitis, erysipelas, gangrene and extensive infection, also the obstinacy of these lesions towards all methods of treatment, make the prognosis dubious. Even though pain and tenderness be absent, the gravity of the condition must be brought home to the patient, and energetic treatment applied early.

Therapy.—This includes the care of the fundamental constitutional disease and the local condition, the tendency to heal depending upon the nature of the former. Unfortunately the basic malady is frequently not amenable to treatment.

Much vaunted as of especial value are remedies such as potassium iodid and mercury. Of other methods may be mentioned the following: constant and induced electric currents, X-ray exposures, high frequency diathermy, and hot air.

Because of the excellent results reported by French and Italian authors (Chipault,¹ Fontana² and Tomaselli³) after nerve stretching, it may not be amiss to record here that the anterior tibial, peroneal, and the larger cutaneous nerves have been exposed and forcibly stretched with a view to influencing the trophic condition.

¹ Chipault, *Presse méd.*, Sept. 11, 1895.

² Fontana, *Riforma med.*, 1910, 22.

³ Tomaselli, *Gazz. d. osp.*, 199, 106.

Local treatment should follow general surgical principles, the value of permanent baths (Chap. LXV) being particularly noticeable in many cases. Surgical procedures depend greatly upon whether there is a communication between the ulcer and the neighboring joint or bone. Excision of ulcers that do not lead to bones or joints has been found reliable in many cases.

X-ray examination will reveal the extent of osseous involvement. When the latter or the contiguous joint is affected, the territory must be adequately cleansed by curettage, or excision of bony fragments on general surgical lines. When only one toe is involved and excessively so, amputation is the best procedure; similarly, when the metatarso-phalangeal joint is diseased.

Whenever, by virtue of secondary infection, extensive disease of soft parts and bone takes place, amputation of larger parts may be advisable. Perhaps the Leriche operation will be of value here (see p. 525).

CHAPTER LXXXIV

EMBOLISM AND THROMBOSIS

Embolism and thrombosis may be considered together, since they are frequently associated in the pathology of gangrene, and since it is often difficult to make a differential diagnosis, or to distinguish between the effects of the pure embolic process and the result of occlusion by thrombosis. In the veins only extensive thrombosis over large territories is effective in producing gangrene of an extremity or portions of an extremity, whereas, in the arteries, either embolism or thrombosis may lead to gangrene.

Emboli may lodge at the bifurcation of arteries, particularly in the popliteal or in the aorta at the division into the iliacs. The source of an embolus must be sought in a portion of the circulatory system, situated proximally to the obstructed vessel, in the left heart and rarely in the right heart, when the foramen ovale is patent. Emboli may be dislodged from the ulcerative lesions of atherosclerosis, from syphilitic arteries, from an aneurysm, or from arteriosclerotic, injured or infected vessels. A heart that is the seat of myocarditis and endocarditis or bacterial endocarditis, or that is altered in consequence of previous infectious diseases, such as typhus, variola, scarlet fever and bacteriemia (so-called pyogenic infection) may be the source of emboli. When the emboli contain organisms, they are called *infectious emboli*, and may give rise to metastatic abscesses.

The cases may be divided into: (1) embolic obturation with insidious course; (2) thrombosis and embolism after infectious diseases, including pneumonia; (3) cases secondary to cardiac diseases; (4) cases following abdominal operations, and complicating pregnancy, in both of which the exact mechanism is not well understood; (5) peripheral thrombotic gangrene,¹ or thrombotic gangrene in healthy or but slightly diseased vessels; (6) embolism and thrombosis complicating arteriosclerosis; (7) embolism and thrombosis complicating acute aortitis; and (8) embolism with aortic aneurysm.

¹ First described by the author, no reference to this type having been found in the literature. However, clinical and pathological investigations have demonstrated the existence of this form.

It must be remembered, however, that a discussion of these forms of gangrene under arbitrary categories must result in overlapping and possibly repetition of classes. For example, acute arteritis of infectious diseases may be complicated by thrombotic gangrene; and on the other hand, thromboses occur in large arteries during acute infections where *no evidence* of arterial inflammation is discoverable. For purposes of orientation and as clinical aids, however, this classification is wilfully permitted.

1. ARTERIAL OBTURATION WITHOUT IMMEDIATE SYMPTOMS

There are cases in which embolic closure of a large artery of the lower limbs may occur apparently without symptoms, for the patient will not remember having experienced anything abnormal in the affected part. Collateral circulation may then become so well established, that there may either be no subsequent symptoms at all, or such as are vaguely described as rheumatic or as local weakness of the affected part. Ensuing secondary signs may be intermittent claudication, tendency to coldness, or weakness of the limb, and a history of poor healing powers. Such pictures have developed under our own observation where one leg had been recently amputated for embolic gangrene. Suddenly, on careful examination, it is noted that the other foot becomes cold, and that the dorsalis pedis and posterior tibial (or even the popliteal) arteries are pulseless; and *yet the patient seems unaware of any local change*. Gradually, the circulation improves, but a certain degree of functional vascular impairment persists. It is in such instances that the future observer may be in doubt as to the nature of the cause of the vascular obliteration.¹ Vascular spasm is not present here, for evidences of lost pulsation persist.

For a further discussion of gangrene complicating infectious diseases, the reader is referred to Chap. LXXVI on Acute Arteritis.

The following instance of sudden arterial blockage is one that may occur unbeknown to the patient in the apparently healthy limb. Here adequate collateral circulation compensates for the circulatory deficiency, and subsequently effaces the symptomatology.

I. L., male, 48 years of age (November 8, 1918) suddenly developed the typical picture of post-pneumonic, embolic gangrene of the *right* foot during his period of convalescence.

Amputation (November 13, 1918) through the mid-thigh by the author for dry gangrene of the foot, the proximal adjacent portion of the leg almost to the knee presenting the picture of moist gangrene.

Dissection of the vessels of the ablated extremity shows that the popliteal artery was filled with red clots, and all of the larger veins of the leg were distended with red blood clots. The walls of the popliteal artery were very slightly thickened, and microscopic section showed some degeneration of the media.

The initial occlusion probably occurred above the point of ablation judging from the nature of the clot at the point of section. This had the appearance of a "tail" clot (Aschoff) or stagnation thrombosis distal to the original point of blockage.

Immediately after leaving the operating room and when he was brought to his bed, the left foot was found to be *cold and cyanotic*, so much so that a diagnosis of blockage of the proximal part of the posterior tibial artery was made. The symptoms gradually abated, and except for the *loss of the pulses* in the dorsalis pedis and posterior tibial arteries, all gross evidences of circulatory impairment completely disappeared.

Embolism Without Gangrene.—Sudden blockage of the popliteal or lower femoral artery is not necessarily followed by gangrene. In cases with cardiac disease, during or after an acute infectious malady, the usual signs of arrested circulation in the territory supplied by the affected artery may

¹ See Chap. LXXXII.

make their appearance; to wit: sudden pain in the calf of the leg or foot, blanching and coldness of the foot, with disappearance of the dorsalis pedis, posterior tibial and popliteal pulses. Through elaboration of adequate collateral circulation, both trophic disorders and gangrene may be averted.

2. EMBOLIC AND THROMBOTIC GANGRENE AFTER INFECTIOUS DISEASES

Gangrene complicating pneumonia may be described as a good example of this type. Sudden thrombosis of the femoral or popliteal artery may occur within a few days (four to eight) or much later (three to four weeks) after the onset of pneumonia. The character of the symptoms, and the extent of the gangrene will depend upon the site of the embolus or limits of the thrombosis; and the general symptoms will be determined rather by the general condition and disease which gave rise to the thrombotic process, than by the gangrene itself, subsequent emboli often causing sudden death.

As early as six to eight days after the onset of pneumonia, or at a much later period, the patient will experience numbness of the foot, coldness, cyanosis, weakness, followed by loss of active motion, and then cyanosis of the distal part. On examination the dorsalis pedis, posterior tibial and popliteal may be found pulseless. Gangrene rapidly ensues, and, if amputation is done, the femoral artery and vein are usually found filled with red clot.

It is often difficult in these cases to determine just where the thrombus began, or just where the embolus became lodged. If amputation is done after the lapse of a week or more, beginning organization of the clot can be demonstrated.

In other cases, thrombosis may occur as late as three to six weeks after the onset of pneumonia, beginning with sudden onset of pain in one limb, coldness and blanching followed by cyanosis, the peripheral arteries being pulseless.

Clinical Course.—Either during the course of the pneumonia, or as a sequel, embolism or thrombosis of the iliacs, femorals, popliteals or brachial may occur. Symptoms of thrombosis or embolism may begin with sudden pain or numbness and coldness in one foot, which rapidly becomes blanched, later cyanotic, the dorsalis pedis, posterior tibial and popliteal pulseless. The typical signs of gangrene then develop, associated with distinct aggravation of the general condition. Where the condition of the patient has allowed it, amputation was done in many of the reported cases. The mortality, however, has been exceedingly high, the patient often becoming delirious then stuporous shortly after operation, or even before amputation was done. The prognosis is grave, either because of the extent of the thrombotic process, and the development of other emboli, or because of the menace of pulmonary edema and heart failure. In some instances, where amputation was postponed for weeks or more, the amputated limbs revealed extensive organizing thrombosis of all the larger arteries and veins.

An excellent example of gangrene of the lower extremities complicating pneumonia is the following.

A. W., 30 years of age, with a history of pneumonia, and with consolidation at the right base, was treated at the hospital in April and May, 1914, having been discharged on the 11th of May. He was again admitted on the 13th day of July because of shortness of breath, palpitation, hacking cough with sputum. On July 25, there was *sudden pain* in the *left leg*, the leg being found cold and cyanotic, with pulses in the femoral, and distal to this artery being absent. Tenderness along the vessels could be elicited. About this time the patient's mental condition changed being frequently irrational.

July 28, the entire left foot was markedly discolored, having a purplish mottled appearance, the whole leg being cold.

August 5, the foot was edematous, swollen. The tip of the big toe was deeply cyanotic, the skin of the rest of the big toe was vermillion red. This discoloration appeared to be due to the fact that the epidermis was lifted off. Over one half of the dorsum there was a large bleb 4 by 3 inches probably filled with bloody serum. All the toes were intensely red, also due to the separation of epidermis. Over the inner aspect of the ankle there was a mild degree of lividity, and behind the Achilles tendon there was an enormous bleb. The red condition extended up to a point 4 inches above the ankle.

In short, the early stage of moist gangrene. The leg was brawny, hard, and very tender to the touch, and especially hard over the calf. This did not appear to be due to superficial edema.

Diagnosis.—Thrombosis of the femoral artery and vein.

August 7, the patient was mentally confused, but rational. From now on the left leg passed through the various stages of gangrene. August 10, 1914, the bluish discoloration and patches of red and blue color seemed to be progressing upward towards the knee and over the outer side of the leg, the temperature of the limb being very low as far as the knee. The redness was still intense over the anterior half of the foot where the skin had been separated, and the foot had increased considerably in size. The femoral artery did not pulsate.

August 12, the whole foot was cyanotic, and in an advanced stage of moist gangrene.

August 15, the limb was much smaller, although the calf was still brawny. The whole leg was exceedingly cold. It presented a variegated appearance due to various changes in different parts of the limb. The foot had a greyish livid appearance, partly purplish and cyanotic. At the ankle there were patches of purple and deep red where the skin had been separated. The discoloration extended to the upper fourth of the leg, and was limited from the normal skin by a zone of purplish discoloration. The fluid having filtered out of the blood, the epidermis being too large, was now wrinkled over all the toes, leaving the tips of the toes bluish black. Evidently the whole foot is in a condition of wet gangrene. The external popliteal vein could be felt as a hard cord. The right foot was edematous, probably due to the impaired cardiac and renal function.

August 24, amputation at junction of the upper and middle third of left thigh.

August 27, very irrational, having marked hallucinations.

September 1, some sloughing of the skin flaps. The patient was removed to another hospital because of his mental condition.

The Gangrenous Leg.—Just before amputation the appearance of the limb was characteristic of the late stages of moist gangrene. Over the foot, the epidermis was completely loosened, lying in folds, torn in shreds in places, the purplish or reddish weeping cutis vera shining through. Higher up over the calf in the anterolateral aspect of the leg, there was a large patch of dry gangrene. The periphery of the gangrenous process, where the demarcation was taking place, showed areas of hemorrhage. (These are undoubtedly very similar to those which we find in early stages of gangrene.) In this process, the blood evidently passed through the capillaries and produced subepidermal or intra-epidermal ecchymoses.

The hardness of the calf was still present, but altogether the size of the foot and the leg was diminished as compared with the early stages of the gangrenous process.

At the time of operation, it was noted that the popliteal and posterior aspects of the thigh were very edematous, and the vessels, arteries and veins, at the point of section, were filled with clots, a red clot occupying the vein, a thicker clot in the periphery, with a whitish center in the popliteal artery.

Dissection of the vessels showed these bound or matted together and filled with red clots. In places the artery was filled with a decolorized clot. Nowhere was there any well organized firm thrombus, such as we see in the later stages of thrombo-angiitis obliterans. The arteries showed a moderate amount of atherosclerosis.

Conclusion.—A case of thrombotic gangrene or embolic gangrene probably beginning higher up in the femoral or in the iliac, extending rapidly down into the popliteal and posterior tibial.

Microscopical Description.—The femoral artery is completely closed by a mixed clot, and shows no evidences of organization. The adventitia and the other layers of the muscularis show slight evidences of a reactive process, there being an extensive infiltration with small mononuclear cells, but only slight migration of polynuclear leucocytes through the muscularis. Here and there wandering cells have reached the internal elastic coat.

The popliteal vein is filled with a bland clot whose periphery is being organized in the typical fashion. The inflammatory reaction here is less marked than in the artery, the only evidences being polynuclear leucocytes in the wall. Some of the small tributaries of the popliteal show more advanced stages of organization.

Types of Gangrene.—When the edema is absent and the veins remain patent sufficiently long, then the characteristic picture of *dry gangrene* results. The initial coldness and pallor are also followed by blueness or bluish purple discoloration. Gradually the peripheral parts are depleted of their water content, and the tips of the toes and outer border of the foot dry up rapidly, gaining the characteristic appearance of the desiccated dissecting room corpse. The color soon changes from the dried beef appearance to a blackish brown, as the process extends up for a variable distance, usually almost to the ankle, rarely much above.

When the condition of *moist gangrene* develops, because of more extensive thrombosis in the femoral vein, and possibly earlier thrombosis in the veins than in the arteries, the following picture of the local condition is typical, but may also be characteristic of embolic and thrombotic gangrene due to other causes.

First Stage.—After a preliminary blanching which rapidly follows the onset of the embolism or thrombosis, the limb becomes intensely cold and soon develops bluish patches that give the limb a mottled appearance (ischemia and cyanosis). The cyanosis becomes intense, spreads rapidly; replacing the areas of pallor; the limb becomes livid and dusky, save for patches of vermilion red scattered here and there.

Second Stage of Subepidermal Exudation.—The foot sometimes becomes edematous, the calf brawny and hard, and extremely tender; the soles are livid or they show a striking vermilion red. Over the dorsum of the foot, large blebs or bullæ form, which contain bloody serum, and some of the toes may become intensely red, because of the separation of the epidermis, the weeping cutis vera shining through. The red condition of the foot extends up for a variable distance to the ankle, or even higher, giving the limb an angry red appearance, characteristic of the second stage of moist gangrene. When edema precedes the gangrene, the brawny and swollen condition of the limb may be intense.

Third Stage of Intense Lividity.—As the gangrenous process becomes more advanced, the bullae become larger; the epidermis hangs in folds, breaks and allows the serum to escape. The color of the skin changes to a deep purple, except for places where the weeping cutis vera still shines through. The general color is often a grayish purple, because of the combination of the dead epidermis and the bluish red cutis vera. Associated with these typical signs of moist gangrene there may be patches of dry gangrene. Higher up, at the periphery of the gangrenous process, where demarcation begins to take place, there are usually areas of hemorrhage, or ecchymosis. The limb above this line is indurated, tender, and usually much enlarged. Sometimes the external popliteal vein can be felt as a hard cord. The popliteal and the femoral are frequently pulseless.

The *final stage of disintegration* has been previously described.

Pathology.—Although it has not been possible in the author's experience to demonstrate the relationship between arteritis and the thrombotic processes in the larger arteries (femoral, popliteal) leading to gangrene in pneumonia, a number of authors describe such acute arteritis as a complication of this malady. Head¹ mentions three cases in which gangrene followed after resolution in pneumonia, and according to the literature, an arteritis was supposed to have existed. In one of these, where a clot was found lodged in the femoral artery, the pathological report described multiple round cell infiltration in the adventitia of the femoral artery.

¹ Head, Am. Jour. Med. Sc., 1921, 162, p. 157.

On dissection of limbs (of pneumonic cases) the vessels are found matted together by intense edema and infiltration. The posterior tibial and femoral arteries are filled with red clot, decolorized in places, but nowhere showing advanced organization, even when the limb is removed eighteen to twenty days after the onset of the thrombosis. Histological examination of such vessels shows a bland clot undergoing early stages of organization. The peripheral layers of the muscle, of the media and the adventitia show extensive infiltration with mononuclear cells. No definite data as to the cause of the thrombosis can be learned from the study of the vessels unless they can be obtained within a few hours after embolism or thrombosis has occurred. In the later stages, the usual signs of organization are present, the organizing process being often older in the veins in the cases of moist gangrene.

In one of the cases of post-pneumonic gangrene described, where dissection was made by the author, vessels of the amputated leg revealed the following: The large vessels (femoral and popliteal) were matted in their sheaths surrounded by considerable edema everywhere filled with red clots. Some of these were found decolorized in places, but nowhere were they firm, nor did they suggest the picture of thrombo-angiitis. The femoral, popliteal and posterior tibial showed these changes. Recent thrombosis was found in other vessels situated distally. Macroscopically one could have concluded that here was a case of either thrombotic or embolic gangrene with the vascular occlusive lesion probably beginning in the femoral or possibly in the external iliac artery, with thrombosis extending rapidly downward.

Histological examination of the femoral and popliteal arteries showed the following lesions: The lumina of the arteries were filled with clots. The adventitia and media were infiltrated with mononuclear cells interspersed here and there by a moderate invasion with migrated leucocytes. The veins, too, revealed similar changes with some organization of the clots.

All these changes could be regarded as being secondary to, rather than as responsible for, the occlusive thrombosis, for the site of the initial lesion cannot be determined in the limited vascular territory obtained by amputation.

Gangrene with Other Infections.—Rolleston reported a case in which a lower extremity was thus affected in a case of diphtheria. He could find but one reported in which an upper limb was involved.

Thrombosis in veins (with phlebitis) has been described as an important and relatively frequent sequela of *influenza*.¹ It is peculiar that both veins of the lower and upper extremities are frequently affected (brachial and axillary). The onset may be very acute and rapidly progressive. The process may be bilateral in large venous channels and may lead to gangrene.

Occasionally venous thromboses of the arm and leg veins may be associated and complicated with gangrene of the foot.² Almost all the veins of the limb may become thrombosed. Closure of one popliteal artery, or of both iliac, femoral, or popliteal arteries with symmetrical gangrene has been described.³ Orth⁴ has reported a case of symmetrical gangrene due to thrombosis of both popliteal arteries; also a case of gangrene of the distal phalanges

¹ Leichtenstern, Deutsch. med. Wchnschr., 1890, Nos. 11, 15 and 18; also Spez. Path. u. Therap. (v. Nothnagel, 4, Wien).

² Johannsen, St. Petersburg. med. Wchnschr., 1890, No. 46.

³ Friederich, Die Influenza Epidemie, etc., Arbeit. a. d. k. Gsundtsamte, 1894, 9, Berlin.

⁴ Orth, Deutsch. med. Wchnschr., 1918, No. 47, p. 1298.

of all the fingers of one hand. A more detailed account of this subject will be found under Acute Arteritis (Chap. LXXVI).

Embolic gangrene complicating *chorea* was observed by Chodak.¹

V. H., aged 12 years, was admitted into the Royal Free Hospital on December 7, 1918, suffering from chorea of a week's duration. This was a first attack, and there was no previous history of rheumatism; no history of shock or overwork. Two years previously she had had diphtheria, with a bad attack of tonsillitis during convalescence. The mother had had rheumatism and one sister has had chorea. On admission the patient, a thin slip of a girl, was found to be suffering from a moderately severe attack of chorea, all parts of the body being affected. There was very little loss of strength on the left side, but the right hand grip was poor and feebly sustained. All reflexes were exaggerated.

Ten days after admission the right hand began to go white, the finger-nails blue, though the hand did not actually feel cold to the touch. The onset may be described as rapid rather than sudden, and it was fully a week before gangrene of the finger-tips and ball of the thumb had definitely set in. During this time the pallor spread up the forearm. There was no pulse at the wrist, but the brachial could be felt pulsating about half way down the upper arm, and after a time there was distinct pulsation of the superior profunda artery.

The temperature throughout never rose above 99° F. and was rarely as high as that. Later still, the brachial pulse slowly disappeared, and the brachial artery could be felt like a thick cord along the arm.

The little finger recovered, and lines of demarcation gradually formed on the remaining fingers. The ball of the thumb appeared at first to have escaped as the discolored skin peeled away from it, but there must have been considerable damage to the muscle, followed by contraction of the scar tissue, which has led to considerable deformity of the thumb.

It was the consensus of opinion of those to whom this case was presented that it was due to embolic gangrene.

Puerperal Gangrene.—Under this appellation quite a number of authors have described gangrene of the extremities complicating pregnancy. Of 76 cases,² 53 involved the lower extremities, 10 the upper. Arterial obstruction through embolism or thrombosis is given as the cause in 29 cases.

CHAPTER LXXXV

EMBOLIC GANGRENE—CONTINUED

3. EMBOLIC GANGRENE WITH CARDIAC DISEASE

When this occurs in young and middle-aged individuals, the source of the embolus is usually the left heart. Autopsy not infrequently reveals thrombi in the left auricle as the probable source, or chronic endocarditis with valvular lesions, particularly mitral stenosis. In the older individuals, particularly the senile cases, with intense athero- and arteriosclerosis and ulcerations of the aorta, a lesion proximal to the site of the embolism, may furnish one causative factor of the embolic process.

The clinical history in cardiac cases is typical and striking. There may be a *fulminating course*, terminating in death within a few hours or a few days (less than a week) after the onset, or a more *protracted course* in which case, the mortifying process in one or both lower extremities or even upper extremities may have progressed so far that demarcation has set in, allowing amputation to be done. Even here, the mortality is exceedingly high, death usually following within a short time after operation.

¹ Chodak, Royal Soc. Med., 1918-1919, Vol. XII (Sect. Dis. Children, p. 87).

² Stein, Surg., Gynec. and Obst., 1916, 23, p. 442.

A typical course of a *fulminating case* is the following: With a distinct antecedent history of cardiac disease, the patient suddenly experiences pain in one or both lower extremities, or pain in the abdomen or back, followed by coldness of one foot or leg, loss of sensation, paresthesiæ and loss of active motion. On examination the affected limb will be found to be blanched, soon after the onset, cold, flaccid, and somewhat tender above the zone of frigidity. The toes soon become livid, purplish or cyanotic, or the ischemic condition of the foot gives way to a mottling, patches of bluish purple appearing over the foot and lower part of the leg. The muscles of the calf of the leg, or the thigh frequently manifest fibrillary twitching. After 48 hours, this mottling gives way to a diffusely livid color, here and there scarlet patches shining through. The zone of coldness and of discoloration corresponds fairly well in extent, the upper portion of the discolored area showing extensive ecchymoses. Death may occur within 24 hours, or within a week, the patient becoming delirious, then stuporous, cardiac failure or cerebral emboli leading to sudden exitus.

In protracted cases dry gangrene often develops; rapid evaporation takes place and the distal parts are the first to become mummified. A type of gangrene which in its objective manifestations can be compared to the desiccating process seen in the drying parts in the dissecting room, is not uncommon. This form of gangrene, when it involves a considerable portion of the foot, or the whole foot, is *almost always due to embolism*.

Where there is a more chronic course over a period of weeks or more than a month, the history may be as follows: With the story of an old cardiac complaint, there suddenly develop shortness of breath, precordial distress, possibly palpitation with or without vertigo and fainting. This is followed by pain in one or both lower extremities, loss of motion and loss of sensation. One or both limbs becomes rapidly cyanotic, the extent of the discoloration depending upon the situation of the thrombus. On physical examination, the dorsalis pedis, posterior tibial and popliteal arteries are regularly found pulseless. The femoral may or may not pulsate. Then the typical changes incident upon the development of dry gangrene ensue. The general condition of the patient will depend particularly upon the cardiac condition, and upon the presence or absence of infection. Usually there is more or less cyanosis due to the impaired cardiac action and evidences of a cardiac murmur.

Such cases may last for a variable time (6 weeks or more) before amputation is done. Although the operation of amputation through the thigh may be temporarily well borne, the mortality is exceedingly high. The patients may suddenly become stuporous. Evidences of cerebral embolus may appear, death occurring within a few hours or several days after amputation.

Embolism at Bifurcation of Aorta.—The following cases taken from the author's files, will illustrate the clinical and pathological findings.

Case I.—*Saddle embolism at bifurcation of aorta with complete occlusion of right, and partial of left iliac artery, gangrene of right lower extremity, amputation, lethal outcome.*

A young woman (M. K.), 32 years of age, Mar. 28, 1912, reports that 5 years ago, soon after childbirth, she had had palpitation of the heart. She was free from symptoms until 8 days ago when she fainted, had shortness of breath and precordial distress. On attempting to leave her bed, she began to have burning pain in both feet and legs, and found that she could not stand. These symptoms were more marked on the right side. Both feet and legs, and to a lesser extent, the thighs, became blue and the patient lost all sensation up to the knee. The weakness in her right leg and foot became so marked that she could not

raise her leg nor move the toes. The same symptoms developed to lesser degree in the left extremity. The right leg and foot have become more and more blue with marked tenderness on pressure over the right popliteal space. The excitement attending her, leaving home, and the transportation caused palpitation, shortness of breath and cyanosis of face and limbs.

Physical Examination.—The general condition was very poor, there being marked cyanosis, dyspnea, some exophthalmos, and dilated pupils.

Heart.—Pulsation seen over mid-sternum; apex felt in 5th space, sounds of very poor quality; irregular action; occasional extra systole with compensating pause. First sound accompanied by systolic murmur, transmitted to left. Pulses equal, small, irregular, of low tension.

Lower Extremities: Right.—Complete loss of muscular power, cyanotic with loss of surface warmth up to a hand's breadth above the knee; big toe colorless. There are ecchymotic patches of varying sizes up to 5 inches in diameter over the extremity.

Left.—Cyanosis up to the ankle joint, and active motion in ankle joint absent.

Vessels.—The femoral pulsation is absent on the right, present on the left. In the popliteal, absent on the right, faint on the left. Both dorsalis pedis pulseless. The lower third of the right thigh hypersensitive, below which part there is complete anesthesia. Knee jerks absent.

April 4.—This A. M. there is marked purplish discoloration up to the junction of the upper third with the lower two-thirds of the right thigh. In the left femoral and the popliteal, there is a faint pulse. The left foot is cyanotic and edematous. The lips of the face are cyanotic, cardiac action being very irregular, a systolic murmur now heard.

Liver palpable, general condition very poor.

April 16.—Line of demarcation just below the right knee, the toes and leg mummified with loss of tactile sensation up to the knee.

May 2.—Circular amputation of right thigh through the middle third well above the line of demarcation. Fat and muscle at the point of amputation looked gelatinous and glassy.

May 5.—Patient is semi-stuporous, occasionally reacts and becomes very noisy, occasionally twitching of extremities, nystagmus, eyes deviating to left. Condition apparently due to cerebral embolus.

May 6.—Patient became stuporous and ceased.

Diagnosis: *Chronic endocarditis* (vegetations), embolism at the bifurcation of the aorta with partial occlusion of the left iliac; gangrene of right leg and impending gangrene of the left, and cerebral emboli.

Pathologic Study of Arteries in Amputated Limb.—The popliteal and femoral arteries especially were sectioned and the complete dissection of the limb made.

Extending from the junction of the upper and middle thirds of the leg and involving the rest of the extremity, there is dry gangrene. This area is sharply marked off from the healthy tissue by a definite line of demarcation. The *vessels, arteries and veins*, as traced in the healthy tissue show thrombi. The muscle tissues seem normal. The fat has a more or less gelatinous appearance. The femoral and popliteal arteries and veins are closed by thrombi.

Microscopically, the walls of the femoral and popliteal arteries show a slight reactive inflammation, due to the beginning of organization of very small portions of the periphery of the clot.

Conclusions.—The vascular lesions do not account for the occlusive thrombosis, and are slight and secondary so that the lesion responsible for the peripheral thrombosis and gangrene must be sought above the point of amputation.

The embolic involvement at the bifurcation of the aorta may be transitory or momentary as the symptoms would indicate, the clot becoming broken up into two parts each, suddenly and violently dislodged and thrown into the corresponding peripheral vessels, usually either the lower femoral or popliteal. When this is the case, we will expect to find both common femoral arteries pulsating (or absent but for a brief period) but both popliteal arteries pulseless. Where there is a saddle shaped aortic thrombus at the bifurcation, all vessels of the lower extremities may be pulseless, or, if there be partial occlusion of one iliac, a faint or moderate pulse can be detected on the corresponding side.

The *history* of transitory aortic embolism with subsequent lodgment of fragments in the peripheral arteries of both lower extremities may be the following: *Sudden onset of severe bearing-down pain* in abdomen and lower

back (oft likened to labor pains) with immediate coldness, pallor and weakness of both lower extremities and inability to use these limbs. Following this comes the advent of gangrene of both legs with absence of pulses in all the vessels from the popliteal downward, the femoral pulses being palpable.

Case II.—Mitral stenosis, onset with symptoms of embolism at aortic bifurcation, subsequently only signs of bilateral embolic gangrene, autopsy revealing absence of clot either at aortic bifurcation or in the iliac arteries.

E. R., age 48 reports that she has had signs of cardiac trouble for some 20 years (prior to Nov. 24, 1915).

Patient has known that she has a cardiac condition for 20 years. She coughs after severe exertion and has cardiac palpitation. During the past 2 weeks she has had severe attacks of cardiac palpitation necessitating her remaining in bed. She arose this morning (Nov. 24) at 6.30 and about one hour later she experienced severe pains in her lower lumbar spine and lower abdomen. The pains in the spine seem to have passed forwards. The abdominal pain resembled "labor pains" and continued for one half an hour. Then a sensation of coldness with the feeling of prickling spread over both legs, these becoming weak and then powerless.

Physical Examination.—Marked cyanosis of lips with red flush of cheeks. A diffuse weak cardiac impulse is palpable, action is irregular and slightly accelerated. At the apex there is a presystolic murmur ending in a sharp short first sound. Pulses are equal and of fair volume, perpetually irregular.

Lower Extremities.—A faint pulsation is felt in both femoral arteries, and no pulsation in both popliteal and dorsalis pedis arteries. The entire right lower extremity feels cold and the foot and leg are blanched. The left foot and leg are cold, the thigh is warm, color of toes is fair, nails are pink. Motion is normal in left lower extremity, whilst there is inability to move the toes and ankle joints of the right leg with preservation of motion in knee joint.

Summary.—*Embolism at bifurcation dislodged into both lower femorals or popliteals with more advanced occlusion of arteries of right than of left leg in a case of cardiac disease.*

Clinical Course.—After the initial pallor of the right foot, a purplish mottling set in, covering the foot and the distal half of the leg, over which region the parts were intensely cold to the touch. After 48 hours this color deepened, the foot and leg became livid and very cold to the touch. Here and there were peculiar scarlet red patches. The small veins of the skin separated the bluish and purplish mottling into irregular areas, and the uppermost portion of the discolored region was somewhat redder. The skin was the seat of diffuse hemorrhages, the bluish green veins being distinctly seen in the ecchymotic skin. Portions of the ecchymotic skin then became dry, whilst others were moist. Above the skin at the middle of the leg the parts were slightly swollen and intensely tender.

The *left leg* was also cold at first. Evidences of gangrene, however, did not set in until 24 hours later, when the leg was cold up to the knee. The foot was then blanched, later mottled, the venous markings being even more distinct than normally, although not prominent, giving the leg the general appearance of a dissection specimen, the numerous veins and venules with their greenish blue blood standing out prominently against the white background, giving the whole surface the appearance of a geographic drawing. Here and there was a pale livid hue extending almost to the knee. Both femorals at this time were pulsating faintly, the popliteals, dorsalis pedes, posterior tibials pulses being absent.

On Nov. 28 gangrene of both legs was well established: exitus on this day.

Autopsy Findings.—Mitral stenosis, dilated left auricle with antemortem clot in auricular appendix; no embolism at bifurcation of aorta, nor in iliac arteries.

Case III.—An exquisite example of initial blockage of the aorta at the bifurcation with subsequent liberation of one iliac due to detachment of the clot, will be cited.

M.M., female, 77 years, had been suffering with recurrent pains in the lower extremities for some four years. When seen by the author (May 5, 1914) she had had a sudden attack of abdominal cramps and pain in both lower extremities with weakness and coldness of the legs nine days before. Some four days later, having been confined to bed since the onset, the legs showed considerable purplish discoloration, and had become quite cold and lifeless. According to her physician, pulsation in neither femoral artery could be detected.

Examination on May 5, 1914.—The right foot is gangrenous, dry, resembling a dried dissecting room specimen; the leg above and up to the mid-thigh is cold and bluish; *the right femoral artery can be felt as a hard cord.*

There is gangrene of the left leg in the early cyanotic and bluish stage up to the knee. *There is good pulsation in the left femoral artery* although none of the distal arteries can be felt.

In view of the bilateral absence of the general pulses at the onset, and the subsequent establishment of good pulsation on the left side, the diagnosis of detachment and peripheral lodgment of clot was warranted.

Diagnosis.—The recognition of embolic or thrombotic gangrene must be based upon the following facts: The existence of the proper etiologic factor (cardiac disease, aneurysm, etc.), the suddenness of the onset with the distribution of the gangrene, the affected territory corresponding to sudden obliteration of one of the larger arterial trunks, popliteal, femoral, and iliacs. The differential diagnosis between embolism and thrombosis cannot always be made, for the gangrene may be due to extensive secondary thrombosis, rather than to the primary lodgment of an embolus in a larger vessel. The mere closure of an artery alone does not account altogether for the extent of the gangrenous process in many instances. Furthermore, the pathological examination of the amputated limb, too, may corroborate the view that secondary thrombosis is responsible for the extent of the lesion. Nor, is it always possible to locate exactly the site of the embolism or thrombosis. Although *simultaneous involvement of both lower extremities* with feeble pulse in the femorals speaks for saddle-shaped thrombus in the iliac, a similar picture may be due to simultaneous lodgment of emboli in both popliteals with secondary thrombosis extending up to the femoral artery. The study of clinical cases, however, together with pathological findings have demonstrated that even where we strongly suspect saddle-shaped embolism at the bifurcation of the aorta, this portion of the vessel may be found free at autopsy. In such cases it may be assumed with some justification, that the saddle-shaped embolus was broken up and dislodged, and thrown into both femorals or popliteals.

When the femoral pulse is lost in both legs, the presence of a saddle-shaped thrombus is almost certain. When there are symptoms in both extremities, and the femoral pulse absent in one, present in the other, a saddle-shaped embolus may or may not be present. If it is, it occludes one iliac more thoroughly than the other. The femoral artery may be felt as a hard cord usually due to secondary thrombosis. The clinical picture may be complicated by sudden exacerbation in the limb which was at first but slightly affected, an argument in favor of the view that another embolus had been cast off in the corresponding vessel. Occasionally embolism or thrombosis of the external iliacs will give the symptoms of ischemia, which will be soon followed by improvement due to the establishment of collateral circulation through the internal iliac arteries.

4. POST-OPERATIVE EMBOLIC OR THROMBOTIC GANGRENE

We are concerned here not with the pulmonary emboli and thrombosis, but merely with the lodgment of emboli in the peripheral arteries, where they may produce gangrene. Surgical operations seem to be a very common cause, or at least seem to provoke, in some way or other, the detachment of emboli in the formation of thrombi in veins and in arteries. Schenk¹ found that of the cases of thrombosis and embolism following operations, 58 per cent occurred after the removal of large pelvic tumors. In 3204 myoma

¹ Schenk, New York Med. Jour., Sept. 6, 1902; also Am. Gynec. Soc., 1913.

operations, 96 or 3 per cent were followed by thrombosis. McLean¹ in his studies of a series of 1310 laparotomies found 26 or about 1.9 per cent complicated by thrombosis or embolism.

The production of gangrene of this type is not thoroughly understood. Doubtless traumatism to the iliac vessels or pressure on the popliteal in the Trendelenburg posture may explain some of the cases; or a complicating cardiac lesion may be the source of an embolus in others. There still remains a fairly large number in which no satisfactory interpretation of the pathogenesis has as yet been offered.

Similarly in the cases of gangrene complicating pregnancy (so-called *puerperal gangrene*), the causal factors have not been adequately clarified. Most of the reported cases have occurred after confinement, a very few during pregnancy and after abortion.

5. THROMBOTIC GANGRENE IN HEALTHY OR BUT SLIGHTLY DISEASED VESSELS

There is still another class of cases in which the etiology of the thrombus formation is not clear, and in which pathological studies have revealed a bland thrombosis of the peripheral vessels, in the territory of the dorsalis pedis and plantar arteries, that is undoubtedly the cause of the gangrene. It may occur in elderly individuals, who have slightly or moderately atherosclerotic vessels, or may occur in vessels that are practically normal save for plaques of thickened intima. These must be distinguished from the cases of thrombo-angiitis obliterans. The specific and characteristic lesions of the latter are absent, and the thrombotic process is less extensive, coming on suddenly, without the long history so characteristic in thrombo-angiitis obliterans. The author has been unable to find a description of this type of gangrene in the literature.

Clinically there is the history of exposure to cold or other insult or trauma. Or, without a cause, one of the toes, usually the big toe, becomes cyanotic; the distal portion of the foot shows areas of blanching. The big toe, or the other toes, may show marked blanching on elevation, or the cyanosis may be so marked that blanching is masked. *Sometimes pain is altogether absent*, another distinguishing feature from thrombo-angiitis obliterans, as well as from the cases of acro-asphyxia. There may or may not be slight erythromelia or reactionary erythromelia. Both lower extremities may be affected, although not simultaneously as in Raynaud's disease. There may be a history of gangrene of one limb, presumably following a mechanical or thermal trauma. Or, no such history may be obtainable. Thus, the first symptom to be noticed may be the appearance of bluish or cyanotic spots or areas at the tips of one or more toes, usually the big toe or the big and adjoining toe. Rather significant, too, is the absence of pain in some of the cases.

Low amputation may not suffice and re-amputation may have to be resorted to in some cases, at the knee or higher.

Pathological studies have revealed that the larger vessels are practically negative, and the small peripheral arteries only are closed. Bland organizing thrombi are found in the territory of the dorsalis pedis and plantar vessels (Figs. 163 and 164). In such cases it is almost impossible to differentiate clinically between chronic acro-asphyxia to which thrombosis has been super-added, slight arteriosclerosis with thrombosis in the distal vessels, or delayed thrombosis following a so-called paralytic functional condition. The last

¹ Jour. Am. Med. Assn., Aug. 29, 1914.

has been described by certain authors (Mönckeberg) as responsible for those late cases of gangrene developing weeks and months after exposure to severe cold (angioparesis).

From the *diagnostic standpoint*, the cases are interesting because they may be confounded not only with chronic acro-asphyxia, but with thrombo-angiitis obliterans and arteriosclerosis. The suddenness of the onset, the sudden disappearance of the pulses, and the rapid development of symptoms,

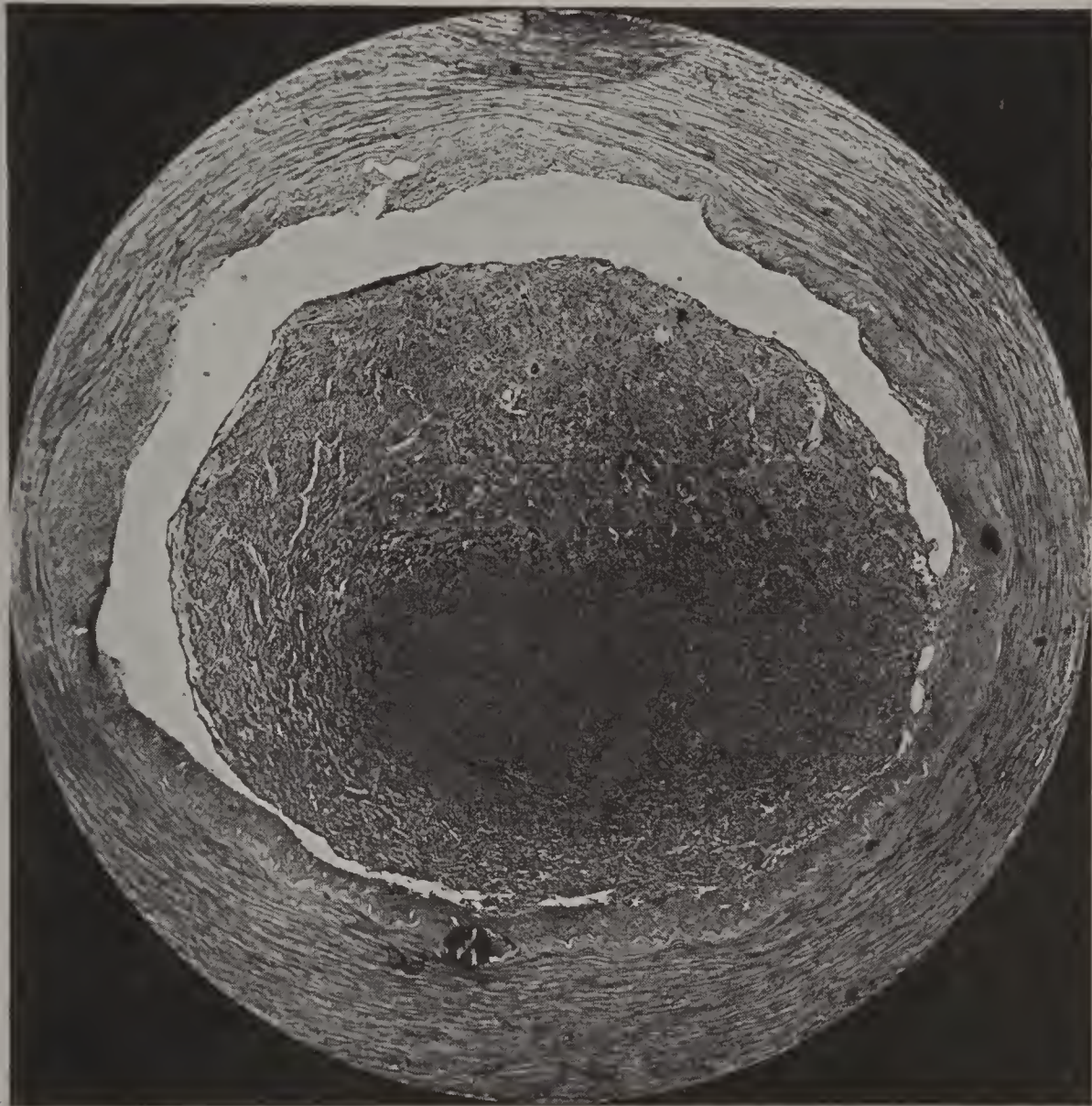


FIG. 163.—Bland thrombosis in slightly diseased vessel.

the absence of pain in some instances, the absence of evidences of marked arteriosclerosis in spite of the age of the patient, are rather characteristic; in thrombo-angiitis obliterans there is a long prodromal period in much more youthful individuals.

Illustrative Case.—A survey of the clinical and pathological findings in a case observed by the author in 1914 will be instructive.

In a man, L. S., 52 years of age (April 1, 1914), who had had none of the premonitory symptoms of arterial disease of the lower extremities, there was a history of exposure to cold with "frost bite" 7 weeks previously. Subsequently, though not immediately thereafter, the big toe of the left foot became cyanotic, *pain being absent*. After some 6 weeks, during which gangrene slowly developed and spread from the big toe across the foot involving all of the toes, amputation was deemed advisable. This was carried out just above the knee. The material for pathological studies thus afforded revealed the following:

The specimen is in two parts, one portion consisting of the knee and upper third of the leg, the other of the remainder of the leg and foot. All the toes and about one inch of the foot above show the terminal stage of dry gangrene. A line of demarcation is well marked.

The branches leading to the internal saphenous vein are all free. The external saphenous vein is filled with postmortem clot. The popliteal vessels are not thrombosed. The wall of the artery is much thickened at the level of the head of the tibia. The anterior and posterior tibial vessels and the peroneal vessels are all free, and show no macroscopic lesion. The dorsalis pedis artery contains a fresh clot which is somewhat adherent to the vessel wall and is dark red in color. In the terminal portion of the dorsalis pedis artery, the clot has a light color and where the metatarsal branch and the digital branch of the vessel come off from the main stem, the clot is lighter in color, and in the digital branch has a yellowish appearance and seems firmly united in the vessel wall. The digital branch referred to arises

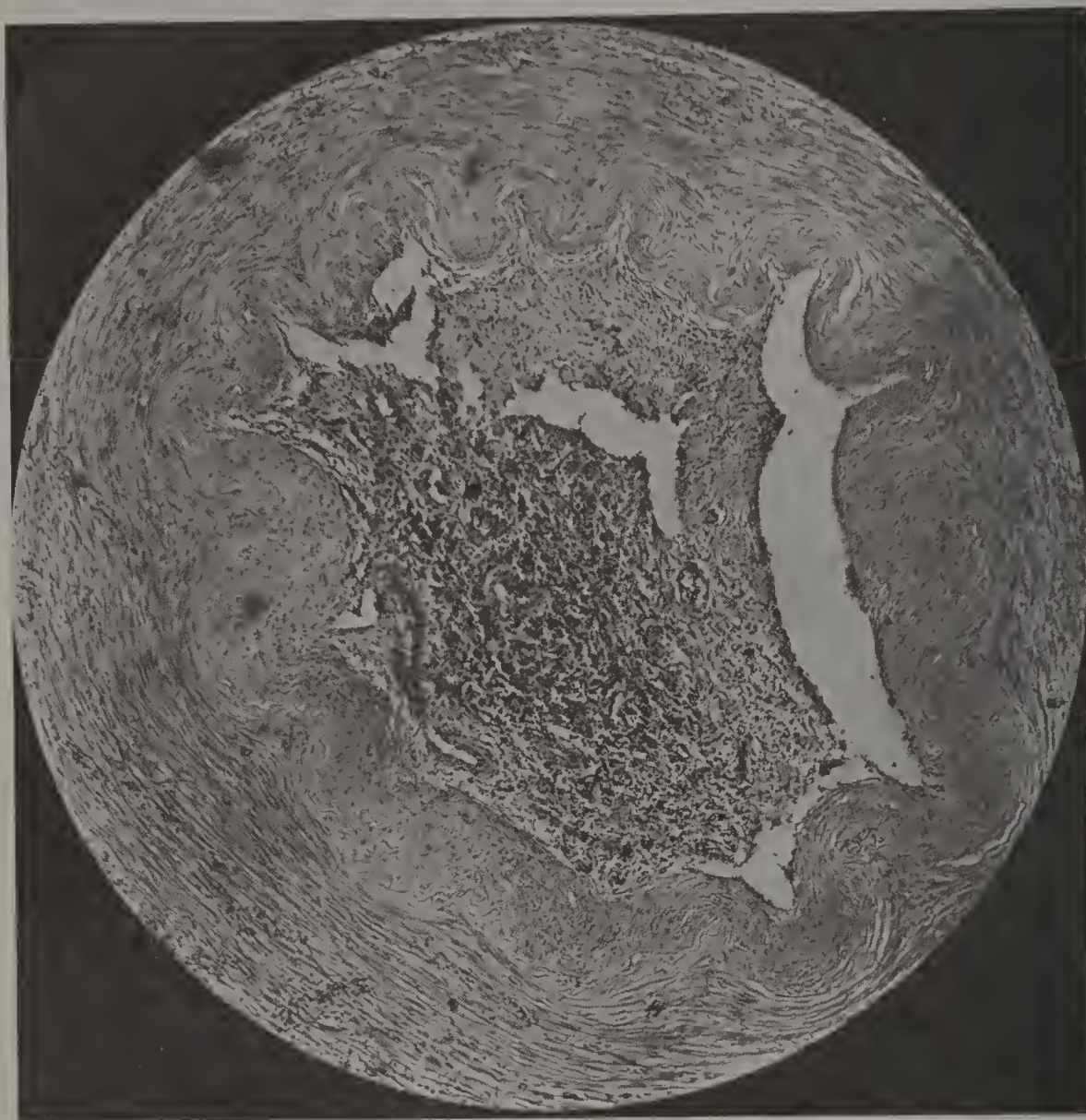


FIG. 164.—Organized bland thrombus in thrombotic gangrene, arteries being seat of moderate degree of arteriosclerosis.

from the main trunk of the dorsalis pedis artery itself. Those branches for the other toes and the terminal portion of the metatarsal artery are all hidden in the gangrenous portion of the foot and toes.

Microscopically the affected vessels showed none of the lesions of thrombo-angiitis obliterans, but the vessel walls were slightly atheromatous, enclosing the "bland type" of occlusive thrombus in various stages of typical organization.

Clinical Course.—About the beginning of July, the big and second toes of the right foot became bluish, being unattended by pain. The cyanosis was followed by formication in this region, and the discoloration persisted for about a month when he was again examined by the author (August 3).

Physical Examination.—August 3, 1914.—The foot was very cold to the touch almost up to the ankle, the tips of all the toes being cyanotic. The sole as well as a portion of the dorsum showed distinct blanching without edema or tenderness. There was a slight increase of ischemia on elevation of the limb without eliciting any pain. A very moderate reactionary rubor was also demonstrable, and differed from that seen in thrombo-angiitis in that it appeared first only and above the ankle from which it extended gradually downward towards the toes. No chronic or constant rubor was present.

The dorsalis pedis and posterior tibial arteries were not palpable whilst the popliteal and femoral were found pulsating.

The symptoms, objective manifestations and diagnostic methods of examination gave data strongly in favor of a repetition of a lesion identical with that of the other already amputated limb.

The chronic cyanosis, the absence of chronic rubor and intermittent claudication, the short duration of the disease before the advent of gangrene, make a characteristic symptom-complex. Occurring in an individual beyond middle age with vessels already slightly atheromatous, the scope of diagnostic possibilities naturally is widened by virtue of the necessity for considering arteriosclerosis as a factor.

From the pathological standpoint, the patent popliteal, peroneal, anterior tibial and posterior tibial arteries with bland thrombosis in various stages of organization in the peripheral arteries (plantar and dorsalis pedis) differentiate this type of case from thrombo-angiitis, and warrant its recognition as a separate entity until further researches will have been made.

Theoretically, lesions of thrombo-angiitis but confined to small parts of the plantar arteries with superadded bland accretion thrombosis, would constitute a pathologic picture beyond the pale of even microscopic recognition. For, the detection of such minimal foci would require a complete study of every bit of the arterial course.

6. EMBOLISM AND THROMBOSIS COMPLICATING ARTERIOSCLEROSIS

Embolism may occur when the larger arteries (particularly the aorta) are markedly diseased. Small thrombi attached to ulceration may become detached and lodged in the more peripheral parts of the circulatory system. In such cases, the symptoms are similar to those described as secondary to cardiac disease. This type may coincide with post-operative embolic gangrene after operation on individuals with the arterial lesions referred to.

Thrombosis of the peripheral vessels complicating arteriosclerosis has been described under the section on arteriosclerotic gangrene. The most characteristic cases are those in which the symptoms of threatening gangrene occur.

7. EMBOLISM AND THROMBOSIS IN ACUTE AORTITIS

Inflammation of the aorta complicating gonorrheal infection is said (Guilain and Rendu¹) to have resulted in gangrene of the upper extremity from "obliteration" of the subclavian artery; and in gangrene of a lower extremity through embolism of the femoral artery.

8. AORTIC ANEURYSM AND EMBOLISM

Gangrene of the leg and feet have been observed as a complication of aortic aneurysm, usually as a sequence of embolism.

The Treatment of Embolic and Thrombotic Gangrene.—The modern approach in the therapy of embolic closure of the vessels of the extremities should be one of operative prophylaxis. By this we mean that every effort should be made to diagnosticate the initial blockage of the main or large artery of the affected limb, and to make accurate localization thereof, so that the thrombus or embolism can be removed in due time, the artery sutured, and the circulation restored. While this is not difficult either from the clinical or operative standpoint, in the case of embolic closure of the axillary or brachial artery, somewhat more acumen and experience are required for the timely and correct interpretation of symptoms due to similar occlusion of the femoral or popliteal artery. An awakened interest and a few germane hints may suffice, however, to stimulate the practitioner to the acceptance of this more advanced and fruitful attitude.

¹ Cit. by Roger and Gouget, *Maladies des Artères*, 1915, p. 370.

The methods recommended for such diagnosis are discussed elsewhere.

The following operative methods have been proposed for dealing with thrombosis and embolism of arteries: First, ligation; second, arteriovenous anastomosis; third, arteriotomy; fourth, arterial resection; fifth, arterial catheterization.

1. *Ligation* has been suggested with a view to avoiding the dangers of embolism. However, Stewart¹ contends that when the diagnosis is certain, thrombosis is usually occlusive, the danger of embolism past; and therefore does not recommend ligation. We are concerned here with the rôle of thrombosis and embolism in the production of gangrene, and certainly ligation can in no way improve the circulatory condition.

2. *Arteriovenous anastomosis* at the present stage of our knowledge seems to be theoretical rather than practical. Stewart believes that in most of the cases reported favorable, even if the arterio-venous fistula remains patent, the blood deflected from the artery into the vein does no more than hinder the return of blood in those veins, producing a sort of passive hyperemia. Stetten,² from his experimental studies, concludes that the operation is dangerous, and the results have been most unsatisfactory, except in a very small percentage of cases, and that even if the anastomosis functionates, which it rarely does, there is no possibility of circulatory improvement, and that the usefulness of the operation is restricted to an unappreciable minimum.

3. *Arteriotomy* (embolectomy) is an operation which must be seriously considered if the diagnosis be made sufficiently early, and if operation be permitted before the effects of occlusion of the vessels have set in, namely, advanced gangrene. Success can only be obtained if the arterial wall is still undamaged at the site of the embolism, and before the secondary extensive thrombosis has occurred. The operation was first proposed by Sabanajew in 1896. Stewart reported a successful case in May, 1907, in a man aged 61, in whom 36 hours after the onset of pain, the femoral was opened, and an embolus extracted and the artery sutured. Pulsation immediately appeared in the femoral below the point of suture, and also in the popliteal, but not in the tibial. Forty-two days later, the leg was amputated below the tubercle of the tibia, and evidences of good circulation were obtained at operation.

Mosny and Dumont³ were able to save a limb by the removal of an embolus 6 hours after its lodgment in the femoral artery. Murphy⁴ removed a clot from the iliac and femoral in a case after gangrene had already set in, making an incision in the superficial femoral. By means of a spoon or scoop and catheter, the clot was dislodged, the catheter passed up into the aorta, a good flow of blood obtained and the artery sutured. He believes that in cases of aseptic embolism, immediate removal by division of the artery in the line of embolism or below should be resorted to. Although in his case he used a spoon and catheter for probing and dislodging the clot, he believes that aspiration through a catheter is a better means of removing the plug. If the catheter be divided on the slant, its open end can be easily introduced into the artery, and, unless the embolism is hard, it can be sucked or drawn into the catheter. He does not advise incision into the artery at the site of the embolism, because this region is already roughened, and the tendency to subsequent thrombosis is favored.

Bauer⁵ has reported a successful case of removal of embolism from the aorta just above the bifurcation through an incision into the artery made by the trans-peritoneal route. The embolus was about 3 cm. long, had the form of a molar tooth with two short roots, these lying in the iliac arteries. The symptoms referable to the lower extremities promptly disappeared, except for some pains in the left foot and calf. This operation, performed 3 hours after the onset, was followed by recovery, the patient leaving his bed on the 25th day.

¹ Ann. Surg., 1915, p. 519.

² Surg., Gynec. and Obst., April, 1915, p. 381.

³ Bull. de l'Acad. de med., LXXV, No. 43.

⁴ Jour. Am. Med. Assn., 1909, LII, p. 1661.

⁵ Zentralbl. f. Chir., Dec. 20, 1913; also Zentralbl. f. d. ges. Chir. u. Grenzgeb., 1914, 4.

The early removal of an occlusive clot from the larger arteries of the extremities—such as the brachial, femoral or popliteal—gives promise of being an effectual mode of coping with impending gangrene of embolic nature. Unfortunately, the practitioner is not aware of the value of immediate surgical intervention in such cases, and the re-establishment of the circulation is hoped for through the mere institution of conservative methods. The condition should be recognized at the very onset of the arterial blockage, and arteriotomy with removal of the clot should be advised.

As soon as the following symptoms are in evidence, arteriotomy should be advised: pain in the affected extremity, coldness of the hand or foot, sensation of the parts falling asleep and formication, interference with motility, loss of sensation, increasing pallor and coldness with or without cyanosis; in short, the usual signs of abolishment of circulation. Coldness, pallor, and absence of pulses may be the only signs.

A typical cardiac case with multiple detachment of emboli demonstrating the value of arteriotomy is the following.

R. S., girl 11 years of age was suddenly attacked with coldness, formication, and pain in the right leg and foot. The dorsalis pedis, posterior tibial and popliteal pulses became imperceptible, but gangrene did not set in because of the rapid development of the collateral circulation (May 25, 1923).

June 8, 1923 it was noticed that the fingers of the *right hand* suddenly became cold. At 8.30 A. M., when seen by the author, the hand and arm up to the upper fifth were found blanched and cold. The brachial, ulnar, and radial pulses were absent, but the axillary and beginning of the brachial artery were pulsating.

At 10 A. M. arteriotomy under novocain anesthesia was performed. On exposure, after dissection of the axillary and upper brachial arteries, the former was found pulsating; the brachial found bluish, and distended with a clot. Careful liberation of these vessels from the surrounding tissues disclosed the fact that the clot extended to the origin of the superior profunda. The brachial and superior profunda were temporarily clamped with a serrefine, and a Crile compressor applied proximally to the pulsating axillary artery. On longitudinal incision into the anterior wall of the artery the clot, dark reddish in color, was spontaneously extruded. To ascertain whether no further minute clots were present, the axillary was allowed to bleed through the incision and then again controlled. Running suture completed the operation.

The circulation in the hand and forearm was immediately restored but the radial pulse remained absent for a few hours, gradually returning to normal. Two weeks later the radial pulse was still normal as well as the circulation of the hand.

It is neither difficult from the diagnostic nor from the therapeutic standpoint to accomplish the localization of the embolus in the case of the upper extremities. Because of the accessibility of the brachial and axillary arteries to the touch and the deductions that perceptible or imperceptible radial and ulnar pulsations can afford us, the recognition of the site of the lesion is easy.

In the case of the lower extremities exact localization may offer a somewhat more intricate problem; but the extent of the coldness of the extremities, its upper limit, and the condition of the dorsalis pedis, posterior tibial, popliteal, femoral and external iliac pulsations may permit us to restrict the possible territory in which the clot may lie to within a very short distance.

The following case is instructive even though the patency of the arterial channels beyond the site of the removed embolus could not be completely restored.

In a young man operated upon for gangrenous appendicitis by a colleague¹ (Feb. 14, 1920), the right forearm suddenly became cold, cyanotic and motionless early in the morning of the third day after the operation. The brachial artery did not pulsate below its upper fifth.

¹ Dr. P. Aschner.

Feb. 17, some $3\frac{1}{2}$ hours after the onset of symptoms, the author exposed the upper portion of the brachial artery at the site of the thrombus, under novocain anesthesia, and by arteriotomy removed the clot, about 2 cm. in length, closing the artery by suture according to Carrel technique. There was excellent pulsation in the brachial below the site of the clot and no leakage after completion of the suture. In spite of this demonstrable patency of the brachial artery below the site of the embolism and thrombosis, *no pulsation* could be detected in the radial artery. It was, therefore, believed that secondary clots had previously become detached and lodged in the peripheral vessels, or had grown upon the embolism (stagnation clots).

Clinical Course.—Feb. 18, in spite of the reestablishment of the circulation in the lower brachial artery, the right hand was somewhat cold, but there was definite evidence of *marked improvement in its circulation*. On Feb. 19, the color of the thumb looked doubtful, being somewhat cyanotic and cold. Furthermore, there were signs of muscular palsy and some tendency to contracture of the fingers in the flexed position. Extension of the hand seemed impossible, although motion of the fingers was excellent.

On Feb. 20, after the application of dry heat in an electric baking apparatus in which a contact burn could have taken place, *trophic disturbances* became manifest over the posterior surface of the forearm. A long whitish area, suggesting dead skin, with loss of sensation over at least 3 inches \times $1\frac{1}{2}$ inches appeared. There was another similar smaller area over the posterior aspect of the wrist and the skin just above. Later in the day, the central portions of these areas showed blebs.

Feb. 25, the fact that a certain amount of gangrene would develop was well established since the following lesions could be demonstrated: First—*The trophic lesions*. Second—*Evidences of gangrene*. Third—*Circulatory disturbances*.

The trophic lesions: The areas of circulatory insufficiency were well demarcated on Feb. 25, there being an elongated area some 3 inches \times $1\frac{1}{2}$ inches surrounded by a well-defined narrow line of deep red, as if a red chalk mark had been drawn around it. Within this there was a distinctly white zone less than 1 cm. in diameter enclosing a central purplish space, in which the typical blebs of gangrene were to be seen.

Evidences of gangrene: The thumb showed a deep purplish color; was somewhat withered, evidently in the early stage of a dry gangrene.

Circulatory changes: Although the postero-external aspect of the forearm was fairly warm, the internal aspect changed color suggesting a possible future necrosis. Between the thumb and the dorsal trophic disturbance, over the thenar eminence and thereabout on the posterior surface, there was a peculiar ham colored red with diminished temperature due to marked circulatory disturbances. The four fingers, however, were in fairly good condition, of good color and the motility good.

Feb. 23—6 days after thrombectomy—slight wrist drop developed, and there were definite sensory and motor phenomena, said by the neurologists to have been due to implication of the ulnar and musculospiral nerves. In the region of the brachial wound there was some induration, possibly due to deep infection.

March 8, chill and rise of temperature to 105.4° with a negative blood culture, the fever disappearing in 24 hours. March 12, again chill and temperature to 106° , and the blood culture showed hemolytic streptococci. March 16, some pus was evacuated from the brachial wound. An abscess of the right thenar space was evacuated on March 18, and on March 20, the temperature gradually attained the normal by lysis.

April 7, the gangrenous area of the thumb had become well demarcated, and the terminal phalanx was disarticulated. A few days later the patient was discharged from the hospital.

In May of the same year the condition of the hand and forearm was as follows: It was atrophic, weak, of a dusky red color, and the fingers purplish. There were trophic disturbances of the nails, which were discolored and poorly nourished. Hyperhidrosis was also present. In the dependent position, paresthesia and pain were very severe. Neurologic examination demonstrated marked impairment of the motor and sensory functions of the median and ulnar nerves. There were still small sequestra at the site of amputation, and these were spontaneously extruded in the course of the next 4 weeks.

Postular exercises and electrical stimulation were given. Improvement rapidly took place, so that in a month the fingers could be semiflexed. Three months later a normal range of motion was reestablished, the atrophy of the muscles was almost abolished, and the color and texture of the skin approached the normal.

It was reported that on Sept. 7¹—7 months after the vascular occlusion—the radial pulse had returned (through collaterals?); one month later the patient was able to resume his work as a chauffeur.

¹ Personal communication from Dr. Aschner.

Although successful from the purely technical standpoint, the radial pulsation was not restored until late, due to the presence of thrombi distal to the site of the embolism. Nevertheless, the operative procedure served a purpose in that an additional part of the brachial became patent, and the source of collaterals thereby widened.

In view of the presence of a bacteremia, there obtained here an additional factor (probably toxic) predisposing to the extension of thrombi. It has been often observed by the author that stagnation thrombosis may spread rapidly from emboli in the larger arteries in cases of pneumonia and influenza, while the field of obturation is more apt to remain restricted and anastomotic paths conserved in pure cardiac disease and atherosclerosis.

The question of removal of the embolus, therefore, should be entertained *very early* wherever an additional toxic element may vitiate the result. In the above case, although the first clinical manifestations of embolism were noted about $3\frac{1}{2}$ hours before the operation, the occlusion was doubtless of at least 10 hours' duration, judging from the appearance of the clot. This may be too late; for, on the one hand, time is given for the detachment of clot through the action of reflux currents and motion of the limb into more remote territories, and, on the other hand, rapid growth of the clot by stagnation, abnormal currents and vortices, and through the forces of ferment liberation, may be expected.

That these factors need not be reckoned with to the same extent in afebrile and atoxic cases, and that the results are more favorable, the citation of an additional case will illustrate.

It is a good example of successful removal of an embolus from the brachial artery and demonstrates that the removal of an embolus about 5 to 6 hours after its lodgment in the brachial artery may be followed by complete restoration of the circulation through the normal vascular paths.

L. G., aged 57, was said to have chronic endocarditis with mitral murmur, there having been a previous history of a number of attacks of erysipelas. About September 14, 1922, he was suddenly seized with a cramp in the right leg, lost consciousness temporarily, but recovered without medical assistance. The right leg became cold, blanched, and gradually darker and darker, developing dry gangrene.

The patient was seen by the author on September 20, at which time dry gangrene involving the greater part of the foot, and moist gangrene over the upper part of the leg had already developed; the lower third of the thigh also being cold to the touch. None of the pulses from the femoral downwards was palpable.

Diagnosis.—Embolic gangrene.

September 21 (8:35 A. M.) a typical circular amputation (without tourniquet) was done by the author through the upper fourth of the right thigh, the femoral artery being found filled with recent clot.

2.45 P. M. of the same day the nurse was unable to obtain a pulse in the right arm; she noticed that the fingers were very cold, the hand pale, and that the patient complained of numbness and weakness in the corresponding hand and forearm. This condition was also observed several hours later by physicians, who recognized the embolic nature of the arrest of circulation in the right upper extremity; but the matter was not reported to the author.

The patient was seen by the author at 7.15 P. M. of the same day, and the following status noted: The general condition of the patient was fairly good; the hand and forearm were cold and pale; neither the right radial nor the ulnar pulsation was perceptible. On palpation along the course of the brachial and axillary arteries, the pulse was found absent below the lower margin of the teres major muscle. The diagnosis of *embolism in the upper brachial artery* was made, and the operation of *arteriotomy* was immediately advised.

After consent was obtained, operation was performed at 9.06 P. M. of the same day.

Operation.—The skin over the lower axillary and the upper part of the brachial artery was infiltrated with 1 per cent novocain solution, and about $2\frac{1}{4}$ inches of the course of the brachial artery exposed in the typical fashion, and the point of obstruction located. At about the level of the origin of the superior profunda artery a clot could be distinctly felt in

the artery, pulsation below this point being absent, and the arterial girth considerably less than that of the vessel above or at the site of the occlusion.

A Crile artery compressor and one *serrefine* were applied above and below, and a small incision about $\frac{1}{4}$ inch in length made longitudinally, immediately over the clot. Just as a compressing and milking movement was attempted in order to force the clot out of the opening, and as a portion of it protruded through the gap, the whole embolus was suddenly projected outward, evidently by virtue of a circulatory force within the artery itself. In spite of the presence of the clamps, bleeding was continuous, copious and non-pulsatile, so that more intensive compression both above and below was applied. As the slit was opened with two delicate forceps, the bleeding which continued in spite of change to the above measures, caused the sudden evacuation of a small shred-like clot, evidently a tail-piece or accretion clot, that had blocked either the superior profunda or was riding upon the embolus in the brachial.

In view of the uncontrollable bleeding through the artificial orifice, it seemed evident that the artery had been opened just opposite to the point of origin of the superior profunda artery, through which a collateral reflux was going on.

It was decided, in view of the importance of the superior profunda as an anastomotic channel, to attempt closure and suture of the artery without tying off this vessel. After thoroughly lubricating the vessel with sterile albolene, the longitudinal aperture was compressed and closed with the thumb and index finger of the left hand. Then arterial suture was begun from above downwards, with the finest silk (doubled) and the finest and smallest Kirby needles (Carrel pattern). Running suture was easily applied, the assistant pulling taut, tying the first knot, the last knot being tied by the operator. After the removal of the clamp not a drop of blood oozed out of the suture line, and it was not deemed wise to reinforce this.

Pulsation and dilatation of the brachial artery below were immediately restored, and the pulsations were confirmed to exist in the corresponding radial and ulnar arteries by an assistant.

Inspection of the fingers and hand immediately after the wound was closed demonstrated a return of color and warmth to the hand and forearm, and restored motility. The patient also noticed a prickling sensation throughout the fingers and hand.

Although the incision in the arm healed by primary union and the pulses were restored and remained so, the patient succumbed subsequently to the lodgment of multiple emboli, one in the left external or common iliac artery, and another possibly in a vessel of the right half of the cerebrum.

On September 28, 8 A. M., the left leg suddenly became cold and blanched, the femoral and the popliteal pulses being imperceptible. From then on the usual manifestations of early gangrene developed, the cyanotic discoloration of the foot and leg, and the coldness which extended up to the groin.

Although the patient was seen about one hour after the lodgment of the embolus in the iliac artery and operation for it was advised, consent was withheld.

September 29, the patient was distinctly weaker, pulse more irregular, and he was at times irrational.

September 30, sudden left-sided palsy, cerebral disturbances, exitus. Up to the time of death, the right radial pulse remained as strong as the left and the circulation of both arms equally good.

In short, a case in which embolectomy with removal of a large clot from the right brachial artery was successfully performed, with restoration of the circulation until death which occurred 9 days after the operation.

Technique.—When the embolism is located in the brachial artery, the following technique will be found useful.

Under novocain anesthesia and sharp dissection, the artery both at the site of the thrombus as well as for some 2 cm. above and below is exposed, kept moistened with saline and lubricated with liquid vaseline. The extent of the thrombus can then be easily determined both visually and by palpation. After the application of a *serrefine* or arterial compressor above and below the clot, a site for arteriotomy is selected either at the very upper end of the clot or over it. A longitudinal incision is made either just above or over the clot with a spear pointed or triangular knife. The clot may be spontaneously extruded, if through collateral branches (or the superior profunda artery) the circulation in the segment within the compressing

forceps is not completely arrested. If necessary, however, and to avoid injury of the intima, the thrombus is milked outward by digital compression above and below. Washing of the artery with saline and longitudinal suture of the artery in Carrel fashion completes the operation.

CHAPTER LXXXVI

THE VASOMOTOR AND TROPHIC NEUROSES—GENERAL CONSIDERATIONS¹

Vasomotor and trophic phenomena may accompany a number of different diseases, such as other neuroses, or organic arterial and nerve affections. But there remains a large group of diseases divisible into distinctly differentiable clinical entities, some of which will be here described under the appellation *vasomotor and trophic neuroses*. A thorough comprehension of all of their manifestations is essential for a diagnosis of the organic vascular morbid processes that they so closely imitate.

The well-known clinical types include the following: (1) vasomotor; (2) sensory; (3) secretory; and (4) trophic disturbances.

The *vasomotor symptoms* may be subdivided into local syncope, local asphyxia and local hyperemia.

The *sensory* include paresthesia and pain, and in certain cases thermoparesthesia and thermalgia are especially notable.

Amongst the *secretory* we group anhidrosis and hyperhidrosis and anomalies of sudoriferous secretion.

The *trophic* lesions are represented by gangrene or necrosis of lesser degree as well as atrophies, hypertrophies, and that unique type of nutritional phenomenon known as *sclerodermal* change.

Distinctive Criteria.—There are sufficiently striking qualities that characterize these groups, and concern (1) the character of the pain, (2) the localization of symptoms, (3) the peculiarities of the clinical course, (4) the etiologic and predisposing factor, and finally, (5) the other signs of involvement of the sympathetic.

1. The pain is never confined to the distribution of a single peripheral nerve or nerve root.

2. The localization is signalized by a remarkable affinity for the peripheral distal parts, as fingers, toes, nose, ear, chin and tip of the tongue.

3. An intermittent chronic *course* which is *not progressive*. This feature is in striking contrast with the progressive course of organic vascular affections such as thrombo-angiitis obliterans.

4. The influence of previous infectious diseases, cold, or other functional neuroses and a neuropathic heredity.

5. The coexistence of instability of the vegetative (autonomic and sympathetic) system, a sort of vasomotor lability, and often vagotonic phenomena.

Not all of these maladies are complicated by gangrene and marked trophic disturbances. Those which can be mistaken for the organic vascular diseases will receive special consideration.

¹ For the latest views on capillary microscopy in these affections see Chaps. CVI, CVII, and CVIII.

The following will be discussed:

(1) *Atypical forms* of vasomotor and trophoneuroses that are intermediary between the well known clinical entities.

(2) Raynaud's disease.

(3) Erythromelalgia.

(4) Acroparesthesia.

(5) Chronic acroasphyxia.

(6) Multiple neurotic gangrene.

(7) Scleroderma.

Although it is most useful, for purposes of clinical segregation, therapeutic indications and prognosis, to follow a grouping of the vasomotor neuroses in some such manner as Cassirer has indicated, we must keep in mind that, as yet, students and investigators of this subject are far from being unanimous; nor are they altogether in accord with the above categorical subdivisions of these disorders. Curschmann¹ will not even admit that *erythromelalgia* merits the distinction of being a discrete malady, and interprets the manifestations as but a single "phase" in the course of *vasomotor neuroses*. Common to a number of these conditions, according to this author's experimental work, is an abnormal type of vascular reaction or an absence of the normal arterial reaction in the affected extremities, when these are exposed to sudden temperature changes.

Employing the plethysmograph, as applied by von Romberg and O. Müller, this author investigated the problem of estimating the arterial response to thermal influences, in 5 cases of Raynaud's disease, 1 case of scleroderma, 3 typical instances of acroparesthesia with erythromelalgic phenomena, 2 cases of angioneurotic edema, and 2 patients with "intermittent claudication."

Müller's researches on the vascular reaction in arteriosclerotic arteries led also to an amplification of our comprehension of what a normal response to cold and warmth should be. Subjecting the proximal portion of the healthy extremity—that which was not in the plethysmographic compartment—to cold, he recorded a sudden diminution in the volume of the distal parts. A similar result followed bodily pain. In arteriosclerotics, this reaction was less marked or absent, in consonance with the intensity of the lesion. Warmth would produce a contrary but slower and inconstant increase in volume.

Adopting this procedure for investigation of the vasomotor neuroses, Curschmann approached this problem, as to whether a continuous or intermittent abnormal vascular tonus exists.

In Raynaud's disease and scleroderma, the normal reaction was absent. Warmth, at times, evoked a *paradoxical arterial constriction*. The conclusion was drawn that a primary disturbance of vascular innervation, therefore, must be a factor in this malady. So also, in his experiments in the *acroparesthesiæ* the normal experimental responses were missing.

We refer the symptomatology in Raynaud's and the allied maladies to the vasomotor system, and to disturbances in the whole vegetative apparatus, and perhaps correctly to the central portions of this system. Organic changes, however, have not as yet been discovered, and doubtless such are not present in the case of most of these affections. The *free intervals* and the *intermittent course* speak strongly against the existence of pathologic anatomic alterations, except in the case of chronic asphyxia and scleroderma.

Some authors, stressing the close interdependence of the vegetative system and the internal secretions, would attribute the manifestations to endocrine dyscrasias. Others consider it more likely that a disorder of the vegetative system is responsible both for the derangement of the vasomotor innervation, as well as for abnormalities of internal secretions.

As mere attendant symptoms (symptomatic form) the manifestations may accompany organic nerve and arterial disease, and hence the confusion and

¹ Curschmann, München. med. Wchnschr., 1907, No. 51, p. 2519.

mistakes in diagnosis that are often made by experienced practitioners even up to this day. *The recognition of the existence of coincidental organic nerve or arterial disease* will do much towards classifying the manifestations as merely *symptomatic*, as opposed to the *idiopathic or intrinsic* complexes that we designate as vasomotor and trophic neuroses and subdivide in the forms indicated above.

Theoretical Concept of the Neuroses of the Vegetative Nervous System.

The clinical manifestations and their mode of origin have been variously interpreted by physiologists and clinical observers. Perhaps the most acceptable views are those according to which disturbances of the function of the vegetative centers are brought into causal relationship with the well-known clinical phenomena. It has been pointed out previously that the center in the corpus striatum may influence the centers in the midbrain in such a manner that the latter (with its subordinate parasympathetic and sympathetic centers) can maintain a certain threshold or state of equilibrium between the parasympathetic and sympathetic functions. Whilst Eppinger and Hess consider the so-called vagotonic complex as an expression of increased excitability of the parasympathetic paths and refer such alterations in irritability to an imbalance between the internal secretions—adrenalin—and an hypothetical “autonomin” (excitant of the parasympathetic), more recent observers would explain the variabilities in the responses of the vegetative system to *changes in the higher nerve centers themselves*. Dresel refers the para- and sympathetotonic disposition or predisposition to functional alterations in the state of excitability of the *corpus striatum*, the latter, as previously stated, containing the regulatory mechanism.

So that increased or diminished adrenalin secretion *per se*, and alone, could not be the cause of a sympathetotonic or vagotonic disposition, as many authors believe. For an increased production of adrenalin should stimulate the midbrain regulatory mechanism in such a manner as to call forth an antagonistic response in other glands, with a view to restoring the old equilibrium. Therefore, it has been concluded that only disturbances in the central nervous mechanism can altogether explain the deficiency symptoms. In short, a true *central neurosis*, or a functional dislocation of the excitability of the corpus striatum would be the more modern explanation of the clinical manifestations referred to derangements in the two large groups of the vegetative paths.

When we attempt to explain the vascular neuroses, it is well to remember that these, just as the other vegetative neuroses (vagetonic and sympathetotonic), may be either of a chronic or paroxysmal type. In the former, would belong the cases of chronic vasomotor lability or instability; in the latter, those in which paroxysms or crises are in evidence, as in Raynaud's disease.

It is well known that there are evidences of functional disturbances of the vegetative system that appear suddenly in predisposed individuals, and then disappear. They may arise by reason of various causes. Both psychic and reflex irritants may play a rôle; and pharmacologic excitation may modify the centers and the peripheral parts of the nervous system. And so, in individuals with certain predispositions (*e.g.*, parasympathetic disposition) minimal excitement, psychic or sensory, may bring about an attack of asthma. In the healthy, such slight irritants may not evoke responses in excess of the physiological. In the vagetonic and sympathetotonic dispositions, with central functional disturbances, paroxysmal symptoms may be brought about through irritants that attack the corresponding nervous system at any point, evoking manifestations in consonance with

the existing hyperexcitability. Perhaps also in the special forms of vasomotor neurosis the well-known crises or paroxysmal appearance of symptoms may be activated by irritants, the nature of which is unknown (toxic, reflex), on a predisposed central nervous system.

Internal Secretions and the Vegetative Functions.—Many data seem to favor the view that internal glandular secretions (hormones) may not only act in a direct fashion, but indirectly through the nervous system. Thus, it was demonstrated that adrenalin exerts the same effect as when the sympathetic nervous system is stimulated. Clinically, too, nervous factors seem to be the exciting causes of many of the diseases of internal secretion, as well as being their most important manifestations. The close relationship, therefore, between the vegetative nervous system and internal secretions seems proven beyond peradventure. Not only does adrenalin selectively influence the sympathetic nervous system, but pilocarpin or physostigmin acts upon the nerve endings of the parasympathetic system in the same manner as electric irritation.

Arterial hypotension has been regarded as a resultant of endocrine disease by a number of authorities since Addison first described epinephrin insufficiency in 1855. A number of different blood pressure states also have been brought into relationship with abnormal activities of the endocrine glands. Numerous publications attest the general proclivity of modern authors to bring into causal relationship certain arterial diseases and those of the internal secretions that markedly affect the non-striated muscle of the vessels with consequent vasoconstriction.

Antagonistic hormones, too, have been recognized as counteracting epinephrin in vasoconstricting effect. Thus the secretion of the thyroid is believed to neutralize or counterbalance the influence of epinephrin, so that certain authorities (such as Weber, Rolleston, and Williams¹) have suggested insufficiency of the thyroid secretion as a cause for the so-called senile, involuntary or decrescent type (Allbutt) of arteriosclerosis. Others take exception to this view.

The importance of thyroid hormones in arterial affections receives further confirmation in the observation that arteriosclerosis is rather a common concomitant of cretinism. Wilson² regards the increased blood pressure frequently following the climacteric as due to the absence of the vasodilating influence of ovarian secretion. Engelbach³ believes that the hypertension in these cases must be due to causes other than the disturbed secretion of the ovaries, or else it would occur in a larger percentage of cases. He offers clinical evidence in support of the theory that a certain selected group of cases of arterial hypertension is associated with endocrine dyscrasias.

Krogh states that a hormone in the blood, probably derived from the activity of the pituitary gland, maintains the "normal" state of contractility of the capillaries.

Mosenthin⁴ expresses the view that in scleroderma we are dealing with deranged internal secretions with increased tonus of the sympathetic, basing his opinion on a study of the vegetative system in one of his cases, and on an analysis of the literature. What glands are responsible, however, he does not make clear. Cases are reported in which scleroderma is attended with disturbances in the thyroid, parathyroid, adrenal, sexual glands and hypo-

¹ Allbutt's Diseases of the Arteries, 1915, I, 230.

² Wilson, S. A. K., Brit. Med. Jour., I, 1261.

³ Engelbach, Wm., Jour. Am. Med. Assn., June 12, 1920, 74, p. 1619.

⁴ Mosenthin, H., Arch. f. Dermat. u. Syph., 1913, Bd. 118, s. 613.

physis. Of late years, there has been a distinct trend to associate thyroid disorders with scleroderma, though it is evident that the glandular malfunction could be secondarily produced, reasoning by analogy, and recognizing that other glands, skin, bones and musculature suffer in this disease. That erroneous conclusions may be arrived at in attributing clinical complexes to certain endocrine disturbances, is illustrated by the case of Rasch,¹ who described a case of scleroderma supposedly influenced or caused by a hypophysis lesion. At autopsy a normal hypophysis but with complete destruction of one of the suprarenal glands was found.

The rôle of the endocrine states in scleroderma is still a mooted question.

Josefson² reports that certain cases of acrocyanosis were cured under thyroid therapy, believing the symptoms attributable to hypothyroidism. In a girl 13 years of age, he also saw improvement after organotherapy. The so-called acrocyanosis associated with tuberculosis is attributed by Rasch³ to endocrine dyscrasia.

Of recent years the pendulum has swung towards the theory of endocrine influences in explanation of the vegetative functions. And perhaps too much importance has been attributed to lesions and derangements of the glands of internal secretion. Conversely, too little weight has been given the rôle of the vegetative nervous system *per se*, which in itself exerts a regulatory control of the activity of these very glands.

As an example may be mentioned the influence relegated to the pancreas in the production of diabetes, and to the thyroid in evoking the Basedow complex. In reference to the former it may be said that Claude Bernard's puncture was proof of the relation of the nervous system and diabetes, and that the sugar metabolism is also influenced through the action of the nervous system upon the adrenal, liver, and muscle cells.

So, too, in the case of essential hypertonia much importance has been attached to the adrenal gland. The rôle of the nervous system has been neglected.

In diabetes Dresel and Lewy succeeded in showing important degenerative changes in the corpus striatum. Experimental work on rabbits developed that the exclusion of the corpus striatum was followed by a permanent hyperglycemia and glycosuria. From this the conclusion was warranted that at least in a percentage of cases of diabetes, localized changes in the brain stem are responsible. Just how these views can be harmonized with the more recent therapeutic results with insulin is a matter for conjecture.

Dresel emphasizes the parallelism between essential hypertonia and the hyperglycemia of diabetes. In the one instance it is the blood sugar, in the other the blood pressure which suffers a rise in threshold. Because of these facts and the observation that even intensive alterations in the vessels themselves may produce no increase in blood pressure in the presence of properly attuned regulatory mechanism, have convinced this author that another explanation must be sought. He offers, therefore, the hypothesis that essential hypertonia is due to a derangement of the central regulatory mechanism, in the sense of an excessively high threshold for blood pressure; and that the arterial changes may be but secondary organic manifestations.

In addition to these *generalized expressions* of central nerve derangements, more *localized* vasoconstrictor effects in circumscribed territories may be referable to central influences. When general, central, or peripheral (parasympathetic or sympathetic) irritation exists, local attacks (of vagotonic and sympatheticotonic nature), such as asthma may result. In the latter affection, psychic, sensory and toxic irritants may be the motivating factors. In the case of angiospastic forms of intermittent claudication a local hypertonic condition of the vessels of the lower extremities may be the response of a functional excitant. (For the theory of the reversal of the normal vasodilating reflex or response to a vasoconstrictor action, through altered

¹ Rasch, C., Dermatologen Kongress, Christiana, 1916.

² Josefson, A., Svenska läkare sällskapets handlingar, 1915, Bd. 41, p. 1.

³ Rasch, *Loc. cit.*

chemistry in the tissues in the obstructive arterial types of intermittent claudication, the reader is referred to Chap. XXVI.)

Internal Secretions and Trophic Disturbances.—With the recent impetus given endocrinology, and the trend to explain numerous skin affections, scleroderma, Raynaud's disease, and the other vasomotor and trophic neuroses on the basis of endocrine dyscrasias, opinions on the relationship of the internal secretions to skin lesions are worthy of mention.

Thus Strandberg¹ in his summary concludes that: (1) the endocrine organs and their secretions have a distinct influence on the integument; (2) that endocrine disturbances can predispose to, and "produce" skin affections; (3) that some of the dermatoses whose pathogenesis is doubtful seem to have a common endogenous cause. Cases of family dermatoses show, not infrequently, a combination of various anomalies of cornification, hair development, nail growth, sclerodermal and vasomotor manifestations.

The Hypersensitiveness of the Vegetative Nervous System.—Clinical observations are being accumulated that point to the possibility of a condition of increased susceptibility or hyperirritability of the vegetative nervous system. It has been pointed out that climatic influences on the organism affect both the function of the endocrine glands, and the vegetative nervous system. Most of the deductions are pure hypotheses, but enough observations are at hand to warrant entertaining some of these. In the case of tetany, the intimate relationship between the endocrine functions and the nervous system seems to have been proven beyond peradventure.

In certain animals, it has been shown that the autonomic nervous system varies in its sensibilities with the seasons. In rabbits irritation of the heat center by acupuncture has proven the varying and seasonal susceptibility of this center. Further data that concern the vacillating irritability of the vegetative nervous system are derived from the clinical observations, that so-called eczema death² and disturbances of the heat center occur in a seasonal way. In the former, a hyperexcitability seems to occur in the spring time, while in the latter, crises or periodic variations in the susceptibility of the vegetative nervous system would seem to take place.

The unusual and interesting disease known as "idiopathic cutaneous atrophy, Erythromelie," has been regarded by some as due to endocrine dyscrasias. A short description of this malady will be found in the chapter on Scleroderma (Chap. C).

CHAPTER LXXXVII

THE SKIN AND THE VEGETATIVE NERVOUS SYSTEM

So important is the control of many of the functions of the skin by the vegetative nervous system, that a general discussion of its influence, and a summary of the nerve paths and of the vasomotor manifestations in the skin may afford an apt explanatory prelude to the clinical description of the vasomotor and trophic affections.

¹ Strandberg, J., Beitr. z. Frage d. Bedeutung d. inneren Sekretion.

² Eczema death is mentioned here as a manifestation of the varying susceptibility of the vegetative nervous system, for it is believed that the cases of sudden, inexplicable death occurring in infants suffering from so-called constitutional eczema, may be due to status lymphaticus, or sudden cardiac paralysis occasioned by vagus malfunction.

The integument in its vascular and other component parts, including the hair follicles, the sweat glands, and the pigment cells, is under the control of the vegetative nervous system. The contractile elements of the skin, the vessels, the hair follicles, and the smooth muscle are affected through *direct stimuli*, namely, by substances that course in the blood and in the tissue fluids; or, *indirectly* through the nervous system. Centers lying in the spinal cord, and governing these functions are in their turn modified and influenced through the quality and warmth of the blood, through psychic impulses, or impulses emanating from the periphery. In this way, vegetative skin reflexes are brought about.

One of the most commonly observed examples of the vegetating functions is the reaction to heat and cold. Whenever, by virtue of external cold, the temperature of the body would tend to drop, a regulatory function is set into action. The vessels of the skin contract, and the blood cannot find its way into the superficial layers of the skin; thus, radiation of heat is prevented. Conversely, with the body overheated, dilatation of the skin vessels takes place, and increased radiation. If this function is inadequate, the action of the sweat glands is brought into play.

In this mechanism, two separate forces or impulses are set into activity: firstly, a direct action upon the vessels and muscles of the hair follicles which contract through cold (reacting contrarily to heat); and secondly, a reflex is set into motion, whose impulses pass through the sensory skin nerves to the vegetative centers in the cord, and thence centrifugally, bringing about contraction or relaxation of the muscular elements of the skin and increased perspiration.

The Vegetative Reflexes in the Skin.—These include the responses that take place exclusively through the route formed by the nerve paths and nerve centers. Two groups have been recognized. In the first group the result of irritation is limited to a territory that closely approximates the region of stimulation. The reflex arc is probably confined here to the spinal cord without participation of the higher centers. As examples may be mentioned the contraction of the smooth muscle of the nipple areola; and the so-called reflex dermatographia.

Whenever larger areas react, we speak of reflexes of higher order (second group). We may mention, to illustrate, the remote action of vasoconstrictor types after cold foot baths, and also the pilomotor reaction that may extend so as to involve a whole extremity or part of the body.

Whenever the reflex becomes still more extensive so as to implicate a large part or the whole of the body surface with chilly sensations and goose flesh, the higher centers (cerebral) are probably at work. Whereas such extensive responses usually require rather severe and intensive irritants, in certain conditions susceptibility may be so heightened that very slight excitation suffices. It has, therefore, been assumed by a number of authors that generalized reflexes are dependent upon certain internal conditions. Given a certain threshold of excitability of the corresponding centers and possibly a certain predisposition of the peripheral vegetative organs, we have the possibilities for reaction to but limited or minimal external influences. With a certain degree of receptivity that is tantamount to a full nerve load, very slight impulses may lead to a discharge; and this explosion, as it were, follows certain existing nerve paths. Secondarily thereto, changes in the innervation of the vegetative organs of the skin may follow.

Alterations in the vegetative innervation of the skin of psychic course (blushing, goose flesh) may expose emotional states no longer under control of the will.

Certain general concepts regarding the lability of the vegetative nerve innervation must be kept clearly in mind for a comprehension of the diseases, such as Raynaud's and erythromelalgia. The skin reactions are subordinate to so many conditions, that we are often unable to draw conclusions regarding the condition of the vegetative nervous system, or, indeed, of the nervous system in general. What may be regarded as a morbid reaction both as regards intensity and feebleness in one case, may still be within the physiological in another case. Many of the conditions that determine the reaction may vary at different times in the same individual; others may be congenital, hereditary or acquired. Of the various coefficients, the following may be mentioned; the condition of the skin, the nervous status, the momentary psychic state, chemical influences (metabolism, internal secretions, auto-intoxication), and so forth.

The Nerve Paths.—The fibers for vasoconstriction controlling the hair follicle muscles over the whole body surface are traceable to the dorsal and three upper lumbar roots, the sympathetic centers lying at corresponding levels in the spinal cord.

The cervical sympathetic contains the preganglionic vasoconstrictor, pilomotor and secretory sweat paths for the face. The vasodilator and sweat inhibiting paths for the face emanate from the cranial autonomic system; for the trunk and the extremities, fibers emanate also from the dorsal and upper lumbar segments that leave the spinal cord through the posterior and not through the anterior roots. In the peripheral sensory nerves of the skin there are fibers for all the constituent functions of the vegetative skin innervation.

It is believed that sensory paths and centers exist for the various skin functions (vasoconstriction and dilatation, pilo-erection and blood secretion), for, these activities are independent.

The vegetative skin reflexes take place through the following reflex arc—the sensory paths constitute the afferent limb of the arc, being traceable from the skin through the skin nerves into the spinal ganglion and posterior root into the spinal cord, then communicating with the vegetative center of the lateral horns. For the vasoconstrictor, pilomotor, and secretory fibers the efferent limb passes through the anterior root, the *ramus communicans albus*, and the sympathetic ganglion through the spinal nerve. The self-inhibiting and vasodilator fibers pass through the posterior nerve to the peripheral nerve. For vegetative skin reflexes of the higher order the interpolation of the center in the mid-brain may be assumed.

The Vasomotor Phenomena of the Skin¹.—Although the mechanism of all the varied pictures presented by or due to active constriction or dilatation of the smaller vessels of the integument is not altogether understood, it may be well to briefly discuss the nature of some of these for a better comprehension of the clinical affections. In the chapter on Capillary Circulation we have alluded to the response on the part of arterioles, capillaries and venules, both to direct influences, as well as to nerve stimuli. The total capillary loop may be affected through the nervous system even by emotion, or externally through cold or other impulse (even mechanical as in dermatographia), active constriction of the loop may result. Thus, narrowing or dilatation of the vascular loops may occur. The greatest fluctuations are noticed in the arterial limbs. Some authors believe that there is a special innervation for the arterial limb in view of the clinical manifestations.

The skin presents either a normal color or deviations therefrom: These are increased redness, transitory rubor, chronic rubor, induced rubor or

¹ For data to be gained from Capillary Microscopy, see Chaps. CVI et seq.

reactive hyperemia, reddish blue cyanosis or asphyxia, complete pallor (syncope), and the so-called marmorated appearance.

The blood content accounts to a great degree for the normal color of the skin, and under ordinary circumstances only a part of the capillary territory is filled. The arterial blood tends to flow rather through the deeper and shorter communicating paths into the venules. When there is hyperemia, rubor or redness, we assume an increased filling of the superficial vascular strata with red arterial blood, with adequate patency of both afferent and efferent channels. At the same time the blood stream is more rapid than normal, and the skin feels warm under such conditions.

The various forms of rubor, transitory rubor of neurogenic origin, or permanent rubor following chronic obstructive arterial disease, and reactive hyperemia (induced or reactionary rubor, or erythromelia) are described in detail elsewhere. Here we need merely mention that a reactive hyperemia may take place in a normal individual after a temporary impediment to the circulation has been withdrawn. And so it is visible as a reactive ischemia due to the application of an Esmarch or Martin bandage, after Bier's method of producing stasis, and after cold or pressure anemias. Opinions vary as to the explanation of this phenomenon, some believing that an exhaustive or paralytic state in the capillaries occurs, others, that there is an active dilatation of the cutaneous vessels. Bier had already suggested the theory that by virtue of metabolic derangement, and absence of oxygen, an active dilatation of the capillaries ensued. This theory is somewhat in accord with the recent views of Hooker who had demonstrated that metabolites or tissue products are capable of inducing an active dilatation of the capillaries.

On the other hand, reflex vasoconstriction in the arterioles and smaller vessels has been laterally interpreted (Zak) as a neurogenic response to accumulating waste products (CO_2), and more properly lactic acid in the muscles; and is assumed to occur in territories poorly supplied with blood after exertion.

Reflex action may also account for the capillary response, as is seen after irritants, such as cold. A livid or cyanotic discoloration of the skin presupposes dilated vessels and stasis. In view of the arrest or sluggishness of the circulation, the temperature of the part also becomes lower, and the skin may become cold to the touch. Neurogenic spasm in the smallest arteries with stagnation in the capillaries and venules (as in Raynaud's disease) may cause asphyxia, or, a combination of circulatory weakness (in obstructed arteries) and the effects of gravity (as in the pendent position), may bring about the same color. Not infrequently can the chronic dilatation of the venules and their immediate channels of higher order be demonstrated in a condition of chronic dilatation, when the cyanotic or livid toes in thromboangiitis obliterans are depleted of their blood by elevating the extremities. Then we note that ischemia sets in because the capillaries cannot be filled in this position, and that the venous paths, either by virtue of dilatation of the venules or vasoconstriction of the larger veins, fail to empty themselves, and remain as livid markings.

Active contraction (vasoconstriction) of the vessels of both skin layers produces complete pallor or syncope.

A reticular patchy lividity or reddish and purplish discoloration of the skin produces the so-called marmorated appearance. We distinguish the livid and the hyperemic form of cutis marmorata. The former occurs usually after exposure to cold. It is not known to what extent a reflex

nervous mechanism, or in how far direct action of thermic influences are responsible.

It is often impossible to segregate the effects of purely vegetative nerve function from the other forces liberated, or already existent in the various morbid entities affecting the vascular system of the extremities. In interpreting the vasomotor manifestations of the organic obstructive diseases, we have to take into account (1) the hydrostatic, mechanical and gravity factors; (2) the central and peripheral reflexes; (3) the reflexes evoked through changes in local circulation (ischemia on elevation); and (4) the local influence of metabolites on the capillary and venule territories.

1. The first of these is discussed in detail in the chapters on Obstructive Arterial Affections. We need merely admonish the clinician, here, that whenever organic interference with vascular patency impedes the flow and diminishes the force of the stream, the state of fulness of the peripheral capillaries and venules is influenced thereby. Indeed, changing position of the limb may alter the circulatory conditions so as to give manifestations of incongruous nature, easily mistaken for those of nerve origin. They may be summed up as being of the nature of *rubor*, *cyanosis* or *asphyxia*, *ischemia* or *syncope*, or simultaneous *combinations* of any of these.

2. The reflexes capable of calling forth alterations of the state of contractility in the vessels of the integument are also referred to elsewhere. For clarity, we may note here that even emotional states and the nervous habitus are not without influence through the higher centers; and peripheral afferent impulses such as cold, motion and trauma are clinically known to produce striking effects.

3. If a limb in which the circulation is impaired through arterial obturation be raised, depletion of the distal surface vessels is produced, and thereby localized ischemia or anemia.¹ Per contra in the hanging position of the limb a condition of rubor, cyanosis or intense cyanosis alone may develop. To what extent are these appearances of purely hydrostatic origin; how far are vasomotor influences at work; and what are the direct effects of local tissue changes or products responsible for the responses in the arterioles, capillaries and venules? These are questions that cannot be categorically answered, but the mere placing of the queries should arouse food for thought, and a correct attitude of interpretative analysis.

Let us analyze but one phase, that of *artificially induced ischemia* on elevation of such a limb. What are the forces besides the hydrostatic, the gravity, the impaired force of the stream that are then brought into play, and that could modify or cause reaction in the peripheral vascular territory?

4. As a result of the depletion, automatic constriction of the arterioles and venules could be predicted in conformance with known laws. But, is there not a simultaneous elaboration of metabolites in such an ischemic territory that would make for dilatation of these paths?² Clinical observation recognizes that dilatation of the capillaries and even of the venules does actually occur. Have the vessels already dilated in the elevated position, and is the pallor merely due to mechanical forces and inadequate circulatory power? Or, does vasodilatation begin only when the limb begins to hang down, and does it require the filling of the vessels to evoke the intensified response?

To answer these questions studies on the morphology of capillaries, and on the capillary pressure in the toes held in such positions, should be made.

¹ See application of these terms by extension, in Chap. X on Local Circulation.

² See work of Krogh, Dale and Hooker, Chap. VII.

And only then will we know which of the forces, mechanical, neurotic or chemical, plays a dominant rôle.

The Cutaneous Responses to Thermic and Actinic Irritants.—It has been observed that rays of long wave length develop warmth energy and act as heat irritants, whilst rays of short wave length, when absorbed, bring about chemical changes. The action of sun rays is well known, the primary hyperemia, the consequent painful reddening, swelling and sunburn. Protracted exposure to light may cause a permanent dilatation of the capillaries.

A moderate degree of heat brings about dilatation of the capillaries of the skin by direct action upon the contractile substance of the capillary endothelium and the musculature of the smallest vessels. It has been shown that the limbs or the neck of an experimental animal when deprived of nerve continuity still respond by a hyperemic reaction to hot air. Very intense heat causes an effect similar to that of cold in the constriction of the cutaneous vessels, particularly in the small arteries. Later, however, with continued exposure a hyperemia of the congestive variety, similar to that produced by cold, is noticed. In this the arteries are constricted, the capillaries and veins dilated.

When severe cold is of but short duration, arteries and capillaries are contracted, and when the external temperature rises again a hyperemic reaction occurs. Continued cold produces a paralysis of the vasoconstrictor action with a livid hyperemia, in which the venous portion of the capillary loop is engorged. In the case of cold, however, reflex action is more apt to take place as is borne out by the observations that a distant part of the body may respond synchronously. As an example, we may quote the contraction of the cutaneous vessels of the other limb when one is plunged into cold water. The immediate effect of cold comprises the action of both a reflex and direct mechanism. So, too, does this obtain in the case of heat (Rehberg and Krogh).

CHAPTER LXXXVIII

DIAGNOSIS AND LOCALIZATION OF VEGETATIVE NERVE LESIONS

The multiplicity of vasomotor centers makes possible the substitution of subordinate centers to compensate for lesions that bring about vasomotor disturbances. This can be all the more effectively brought about, in that the minor centers have a greater independence of action than the superior. On the other hand, this far-seeing provision of Nature has its draw-backs. For the recognition of the seat of lesions of the vasomotor system is consequently made difficult, and oft impossible. The existence of two systems of contrary powers and their susceptibility to varied reflexes from all over the body still further complicates diagnostic work. One may conclude, therefore, that it is quite impossible to make deductions regarding the pathogenesis of vasomotor disturbances from their character and distribution. Perhaps only where the vasomotor derangements are closely limited to the course and distribution of certain peripheral nerves, can we diagnosticate the seat of the lesion.

Deficiency symptoms in the vasomotor system show great tendency to recovery, a fact that is easily explained by the substituting action of numerous other centers. On the other hand, however, when we are dealing with the results of irritation of such centers or paths, other centers cannot act as surrogates, and no compensatory action takes place. With continued irritation we do not expect any abatement of clinical manifestations until the excitability of the corresponding nerve segment ceases and is followed by paralysis. For an understanding of the clinical cases of vasomotor disturbance, we must remember that through reflex paths irritation of the vasomotors can persist for a long time. So, too, it is observed that irritation within the vasomotor system has a more potent action than the paralytic causes. Therefore, whenever we see vasomotor symptoms of long duration, we should look to reflex irritation as possible causes rather than to paralytic conditions.

Although no final knowledge regarding the localization of lesions in this domain is at hand, some of the salient facts that clinical observations and pathological conditions have furnished may be worthy of recapitulation.

Cerebral Lesions and Localization.—Vegetative disturbances following lesions of the cerebrum with motor and sensory symptoms regularly occur on the contralateral side. This would indicate that vegetative fibers, as well as motor and sensory fibers undergo complete crossing on their way to the periphery.

It is well known that in those cases of Brown-Séquard palsy, where the lesions reside in the cervical cord, the vasomotor paralyses take place on the side of the lesion. And so it is assumed (Depisch) that the crossing of the vegetative paths occurs somewhere between the thalamus and the cervical cord.

Vasomotor disturbances on the opposite side are reported as resulting from operations on the brain (Schlesinger¹). Nothnagel also describes such derangements complicating cerebral lesions.

Rossolino² reports a case with attacks of Jacksonian epilepsy attended with edema and a livid discoloration of the affected upper and lower extremities. The temperature of the hand was 2–3° C. lower and the temperature on this side of the body was also 1° lower. At operation a cyst was found in the anterior frontal gyrus of the opposite side, and after evacuation of the cyst the motor power of the extremity, which had been diminished, and the circulatory phenomena returned to normal.

In a study of the vasomotor disturbances in hemiplegia, Goldstein and Parhon³ found in 13 out of 18 cases diminished temperature on the paralyzed side; in 4 no differences.

Mager⁴ describes a bluish discoloration of the skin below the middle of the paralyzed leg with lowering of the skin temperature in a case of right-sided hemiparesis. Autopsy showed a small apple sized-tumor involving the lower part of the central convolutions.

Deficiency symptoms in cases of disease of the cerebrum, where large ganglia are implicated but not wholly destroyed, are associated with disturbances in the vegetative processes of the contralateral side in the form of paralytic or irritative phenomena.

Amongst the paralytic symptoms may be mentioned palsies of the ocular sympathetic and palsy of the vasomotors; of the irritative symptoms, occasionally mydriasis, increased constriction of the cutaneous vessels, increased secretion of sweat, the salivary glands, and mucous membrane.

The vegetative paths crossing in the medulla oblongata for the eye, the vasomotor and sweat glands of the face are believed on the other hand to

¹ Schlesinger, Arch. f. Dermat. u. Syph., Festschrft. Kaposi, 1900.

² Rossolino, Deutsch. Ztschr. f. Nervenhe., 1895, 6, p. 76.

³ Goldstein and Parhon, La Roumaine med., Apr., 1899.

⁴ Mager, Vide Obersteiner, Arbeit. a. d. neurol. Inst., 1907, XVI.

connect directly with the same side of the body. The crossing point of these fibers, therefore (Breuer and Marburg¹), would have to take place between the pons and the internal capsule.

The Vasomotor Paths for the Trunk and Extremities.—The cases of apoplec-tiform bulbar paralysis would seem to indicate that the crossing point of these fibers lies somewhat lower than that of the vegetative paths for the face.

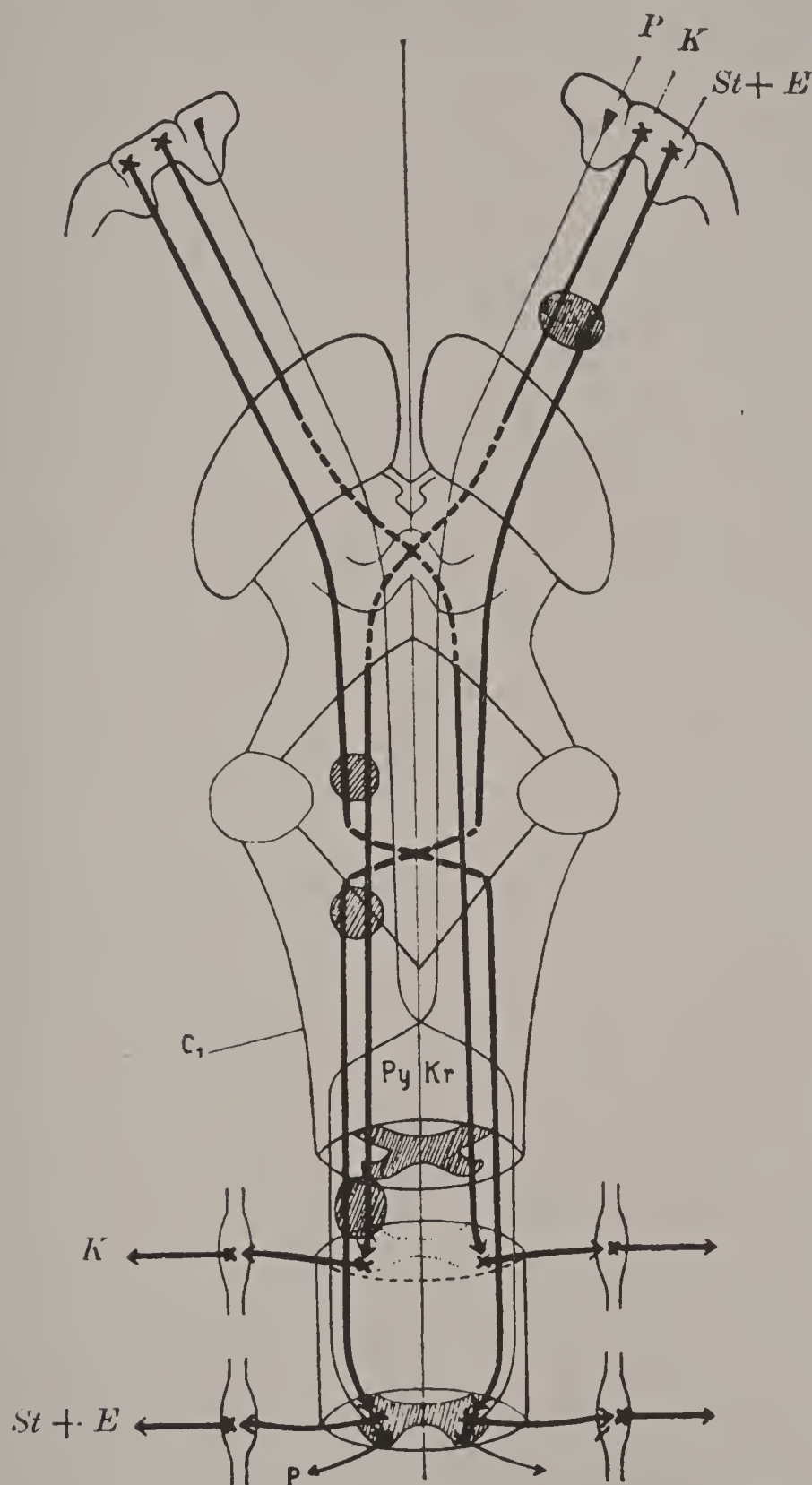


FIG. 165.—Decussation of vegetative nerve paths. (After Depisch)

P = pyramidal paths

K = vegetative paths for the head

St + E = vegetative path for the trunk and extremities

For, the clinical cases demonstrate that the vasomotor lesions occur on the contralateral side (Fig. 165).

For elucidation of diagnostic interpretations the following recent views concerning the cerebrospinal vegetative paths may be of some value. They

¹ Breuer and Marburg, Quoted by Depisch. Wien. Archiv. f. inn. Med., 1920, I, p. 191.

may serve as an aid to localization when additional data will have been forthcoming.

1. The vegetative paths from the cerebrum and the large ganglia of the brain-stem undergo a crossing on their way to the periphery.

2. The decussation is complete at a level of the lowermost portion of the cervical cord; and below this the fibers undergo no further crossing.

3. The decussation of the paths of the ocular sympathetic and of the vasomotor and secretory (sweat) impulses is accomplished in the region of the pons.

4. The crossing point of the vasomotor and secretory paths for the trunk and extremities would appear to take place somewhere in the neighborhood of the pyramidal decussation.

In short, these vegetative paths cross lower than those of the head, though higher than the motor fibers.

These facts are in consonance with the clinical observation that either crossed or homolateral disturbances of the vegetative function can occur in lesions of the superior cerebrospinal tract.

There would, therefore, be a region in which lesions would implicate vegetative paths before any decussation takes place and with homolateral derangements as a sequence.

Pharmacologic Tests of the Vegetative Functions.—The three poisons, adrenalin, pilocarpin and atropin, are mainly used. Of these adrenalin acts on the whole sympathetic system; pilocarpin only on part of the parasympathetic. The latter may be regarded as a substitute for that hypothetical substance—autonomin—which, according to Eppinger and Hess, normally keeps the parasympathetic nerve endings in a constant state of excitability.

Adrenalin is a poison that acts as an excitant on the points of junction between the sympathetic nerve endings and the end organs (myoneural junctions). Tests for the production of general or local symptoms have been evolved, with a view to estimating the irritability of the sympathetic system.

Injection of adrenalin (1 cc. of 1:1000) subcutaneously causes normally the following reaction: after a few minutes palpitation, feeling of distress and tremor of the extremities, and local pallor and blanching of the face ensue. In individuals whose sympathetic system is hyperexcitable, the reaction is excessive; the whole body may shake, there being precordial distress, cardiac pain, perspiration and even transitory collapse.

Persons whose parasympathetic system is over excitable suffer little or no reaction after adrenalin injection. However, by reason of the inordinate vagus response, these individuals show numerous extra systoles.

A reaction of excessive glycosuria is also regarded as a sign of hypersensitiveness of the sympathetic; absence of such, a vagus susceptibility.

Responses on the part of the blood pressure, too, have been interpreted as of value in this connection. A rapid reaction with an abnormally high adrenalin blood pressure curve is said to be characteristic for a hypersensitive sympathetic system.

Loewi believes that mydriasis following the instillation of 1–3 drops of a 1:1000 adrenalin solution in the conjunctival sac indicates defective tonus of the vagus or hypersensitiveness of the sympathetic.

Pilocarpin, since it excites the parasympathetic system, is employed to estimate the responsiveness of the latter. The reaction after subcutaneous injection of 1 cc. of a 1 per cent solution is observed. The normal effect is a feeling of heat, perspiration, redness of the face and increased salivary

secretion. When the reaction is excessive, it indicates an increase of the irritability of the parasympathetic system, or generalized hypersensitiveness of the whole vegetative nervous system.

Atropin has been used to detect the influence of the vagus on arrhythmia.

If symptoms supposedly due to over excitability of the vagus disappear after atropin injection, then confirmation of their vagus or parasympathetic nerve origin is at hand.

CHAPTER LXXXIX

VASOMOTOR AND TROPHIC DISTURBANCES IN LESIONS OF THE CENTRAL NERVOUS SYSTEM

Intensive emotions may in susceptible individuals be followed by the appearance of pruritus or urticarial types of eruption. It is well known that severe shocks or psychic insults may cause the hair to turn grey, and a partial or total alopecia may result. Paroxysmal or long continued swelling of the skin may occur upon the paralyzed side after cerebral injuries—expressions of vasomotor disturbances—and even ungual dystrophies and anomalies of hair growth may complicate. Almost all the forms of trophic disturbances may be associated with spinal cord diseases.

In *myelitis* we occasionally find bullous eruptions and herpes zoster. During paroxysms of tabetic origin, crises of herpetic eruption or urticaria or purpura have been observed.

Herpes zoster is regarded as a reflection of disease of the spinal ganglia; an expression of abnormal increased excitability of the peripheral sensory neuron, or more probably of the peripheral vasosensory motor neuron. It may also attend lesions of the sympathetic gangliated cord.

Tabes Dorsalis.—Trophic disorders here will hardly be confounded with the vasomotor and trophoneuroses, except in the case of associated malum perforans. Spontaneous gangrene has also been reported as complicating this disease. As a rule muscular atrophy involving large muscle groups, trophic affections of the joints and bones, and the so-called tabetic arthropathies are the well-known evidences of trophic derangement.

Syringomyelia and Gliosis Spinalis.—The manifestations of disturbed nutrition are exceedingly varied, very often in the form of small vesicles or larger blebs over the hands. After rupture of the blebs, indolent ulcers develop. Wounds and cicatrices so often encountered over the hands of these cases are usually due to an inability to perceive pain and thermic impulses, and hence burns readily occur without the knowledge of the patient. Remak, Schlesinger and Oppenheim describe reddish blue discoloration of the hand and forearm (vasomotor phenomena). More extensive trophic disorders may take the form of bone necrosis, destruction of the terminal portions of the digits; or, if infection supervenes, phlegmonous processes may be expected.

A peculiar appearance of the hands with enlargement simulating that of acromegaly has been observed (Schlesinger, Oppenheim). Even a myxœdematous change in the skin may be associated. Marinesco is responsible for the term "*main succulent*" as descriptive of a striking alteration in the consistency and texture of the soft parts of the hands. A diffuse swelling especially of the dorsal aspect sufficient to mask the underlying bony and other

landmarks, often attended with vasomotor phenomena, is regarded as characteristic. By virtue of muscular atrophy, a narrowing of the hand may take place. Arthropathies are frequently associated.

A consideration of these manifestations will facilitate differentiation from the other forms of vasomotor and trophic neusosis (Chap. XCIX).

Injuries of the Spinal Cord.—The relationship between the nature of the vasomotor disturbances and the character and extent of the spinal cord lesions has not been definitely established. After total transverse lesions extensive vasomotor palsy of regions below the level of injury are often seen. They may, however, occur after incomplete interruption in continuity of the cord, and may be present in spastic conditions. Even so-called “vasomotor disturbance of the lymph system” has been described by Marburg and Ranzi, reflected in the condition of pasty swelling of the leg, following spinal cord lesions. With the vasomotor disturbances there may be trophic disorders, decubitus, vesicle formation and ulcers.

These authors describe the following picture: The legs are swollen, the skin tense and stretched, glistening, of a waxy white color, occasionally bluish, the skin devoid of the usual characteristics of edema; or occasionally, too, edema, cyanosis, and coldness of varying degrees are observed.

Vascular dilatation may appear over the paralyzed region; later coldness and cyanosis, signifying chronic vascular relaxation. Vasomotor disturbances are also responsible for the engorgement of the corpora cavernosa in such cases.

In Brown-Séquard's symptom-complex (unilateral transverse lesion) the skin may be reddened and warmer on the same side; later on, this may give way to a chronic condition of coldness and cyanosis. An interruption of the vasoconstrictor fibers of the lateral column of the same side is given as the explanation therefor.

Decubitus may occur rapidly after traumatic lesions of the spinal cord. Kroh saw it develop 18 hours after injury; Henneberg on the morning following the trauma; and Krause emphasizes the unfavorable significance of its rapid advent. Decubitus may occur in places that are not subject to pressure. Total transverse lesions of the cord are not necessary for the development of such lesions.

Two factors deserve recognition as of etiologic importance in the neurogenic type of decubitus; namely, alterations in the circulatory function of the affected parts, and the direct influence of pressure, which, in most instances at least, is a factor. Nevertheless, the occurrence of acute decubitus with central nerve lesions has been so frequently described by competent observers, that a mechanical, traumatic or pressure effect has been proven to be not essential.

CHAPTER XC

NEUROTROPHIC DISORDERS IN SPINA BIFIDA

Syringomyelia and spina bifida occulta may be complicated by trophic lesions that should not be confounded with those due to impaired circulation. Those associated with spina bifida occulta may occasion doubts as to diagnosis. These, however, should be easily dispelled if we remember that in the latter, the arterial pulsations are normal, that sensory derangements of

the lower lumbar and sacral nerve roots or segments are usually present, and that true gangrene is absent.

We are interested here merely with those vasomotor and trophic manifestations that may lead to difficulties in differential diagnosis. A short resumé of the salient features of the affection, however, may clarify doubtful points.

Spina bifida occulta is said (Recklinghausen) to be attributable to an intrauterine healed myelomeningocele. According to this theory there should be a defect in the dura, but this is not always present. Hair growth and tumors are frequently found at the site of the defect in the spinal column. This manifestation is explained by the fact that in intrauterine life tissue elements are displaced. According to other authors (Marchand) cystic dilatation with spina bifida exists in intrauterine life with healing and spina bifida occulta as the end product. The existence of mixed tumors, fibromyomata, myofibromyomata is explained on the assumption that an intrauterine myelomeningocele, the product of the healing process in spina bifida occulta arises; and that through the traction of the scar, the skin, musculature and connective tissue become transferred or displaced into the depth and even into the spinal canal; from such, elements of neoplasms may arise.

Symptoms of Spina Bifida Occulta.—These may be divided into: (1) those at the site of the sacral cleft; (2) those resulting by reason of involvement or lesions of the spinal canal contents, namely, the cauda equina, and the nerve roots and peripheral nerves.

We are concerned only in this connection with the sensory, vasomotor and trophic disturbances. The latter will receive detailed consideration, whereas the other symptoms will be given merely passing mention.

1. *The Local Symptoms.*—Of these the abnormal hypertrichosis is the most important, being noticeable in the region of the cleft. Cicatricial changes in the skin, with elephantiasis deformation, dimples, telangiectases, localized hyperhidrosis, funnel-like retraction of the skin or pseudo fistula formation, or abnormal depressions on this region—all these should arouse the suspicions of spina bifida occulta. But in many cases a sacral deficiency may exist even under normal skin.

Occasionally a small *tumor* may be felt under the skin, which in itself is suggestive of spina bifida occulta. Any tumefaction in this region should arouse suspicion of the existence either of a spina bifida vera, or cystica, or one of the occult or concealed variety without protrusion of the contents of the spinal column. A tense elastic consistency would point to the former, a lobulated more solid nature to a lipoma over an occult variety. Local subjective symptoms include, vague pain, particularly on changing the position of the body or on exertion, probably due to traction of the cauda equina or nerve roots.

2. *Nerve Lesions of the Cord or Cauda Equina.*—From the diagnostic standpoint it is valuable to know (Müller) that sensory irritative symptoms are absent when the lower part of the spinal cord is diseased, but paralytic symptoms are present, the latter in part as disassociated sensory phenomena. When alteration occurs in the cauda equina from compression due to a tumor or from traction, sensory, irritative manifestations are intense, and paralytic symptoms for all sensory qualities appear simultaneously.

From the therapeutic and operative standpoint, it is important to determine whether the cauda equina is mostly involved. For in the latter case, more is to be expected from therapy. Indeed, the cauda is capable of undergoing some regeneration after operative work. Müller believes that when the trophic centers for the motor fibers in the spinal cord and the trophic centers for the sensory fibers in the spinal ganglia are conserved, regenera-

tion of axis cylinders and medullated sheaths may occur after the deleterious forces in spina bifida have been put into abeyance.

Disturbances Due to Lesions of the Nerve Apparatus.—These comprise neuralgia, pain in the region of the cleft, irritative or paralytic symptoms in the perineal region, genito-urinary apparatus and the lower extremities. It may not be necessary to give a detailed account of these here, since they are well known, resulting from congenital degenerative processes. Club-foot, pes cavus, trophic disorders of the lower extremities, particularly of the feet, and bladder symptoms, particularly enuresis, are amongst the most common manifestations.



FIG. 166.—Trophic ulcer in the plantar aspect of clubfoot in a case of spina bifida. (Beck)

Vasomotor and Trophic Disturbances.—Sensory disturbances of varying intensity, not always confined to the territory of certain nerves, usually coexist with other deficiency symptoms. There may be either irritative or paralytic symptoms. Sensibility may be either diminished, or tactile anesthesia, especially for pain and temperature, may occur. Usually the hypesthesia or anesthesia is limited to the foot or a part of the foot, or to a small territory over the leg or thigh. The various sensory disturbances may not be equal, inasmuch as tactile sensation may be conserved coincidentally with diminution or absence of temperature and pain sense. Or, the usual symptoms of cauda equina lesions may be present, with the typical saddle shaped area of anesthesia, sometimes attended with paroxysmal pain. Diminished pain and temperature sensation is rather characteristic for spina

bifida occulta. In the mild cases sensory disturbances may be slight or absent. Irritative phenomena and neuralgias indicate participation of the cauda.

As for the *vasomotor and trophic derangements*, these are usually limited to one lower extremity comprising bluish red discoloration of one or both lower extremities or parts of the extremities, involving the foot or leg, and atrophy of an extremity with poor development of muscles of the whole leg.

Mal perforant is considered one of the characteristic manifestations (Fig. 166). Complicating this condition osteomyelitis, sequestra, necrotic bone particles, loss of toes, with consequent deformity of the foot and phlegmonous processes, have all been described. Amputation is required in a number of cases, after which healing may be poor. Secondary ulcers may necessitate reamputation. Ulcers may appear even in more central parts.

Motor disturbances not infrequently accompany the above, with slight paresis or weakness of the single muscles, and even extensive paralytic complexes; more rarely irritative motor phenomena, such as fibrillary twitchings and spasms.

An instructive case reported by Brickner¹ is worthy of brief citation, for the type of trophic lesion is well exemplified.

S. H., female aged 18, presented herself for examination December, 1907, because of an extensive ulceration of the inner and flexor aspects of the great toe of the left foot, indolent in appearance and with foul discharge.

She was a native of Jenkoping, Sweden, where at the age of 7 the second left toe was ulcerated from what was presumed to be frost-bite. This ulceration recurred each winter, and at the age of 12, partial amputation of the toe was required.

Three years later (aged 15) the stump of the toe ulcerated and the phalanges necrosed. Six months later the fifth toe ulcerated, refused to heal, and was amputated. The first phalanx was necrotic. The wound was laid open and this bone was removed. Slowly the wound healed, *without granulating*, after the head of the first metatarsal spontaneously discharged. Specific medication seemed to exercise no influence. The dorsalis pedis, popliteal and posterior tibial vessels pulsated normally.

In April, 1908, the two remaining toes (third and fourth) ulcerated and the two last phalanges of these were removed, leaving stumps. The foot was then quite edematous, but not painful, although there developed at this time a plantar ulcer near the base of the third toe.

Over the lower lumbar and upper sacral regions, extending down from the third lumbar vertebra is a circular tumor about $4\frac{1}{2}$ inches in diameter, symmetrically situated over the midline. This tumor was present since birth and has grown with the patient. In the spine no cleft can be felt. Tests show sensory paralyses of the left lower extremity. Roentgenogram shows a cleft in the *left* lamina of the fourth lumbar arch. The fifth lumbar arch is not of normal shape.

Clinical diagnosis: Spina bifida occulta associated with congenital lipoma over the lower end of the spine; cleft in the fourth lumbar arch with a lesion involving the posterior fourth and fifth lumbar, and first, second and third sacral roots or cord segments.

Operation, July 3, 1908: The sac was removed, the nerve roots were reduced into the spinal canal, and the dura was sutured over them. The lumbar aponeurosis was closed over the hiatus by a plastic operation.

The ulceration in the third toe had progressed and the plantar ulcer had also increased in size, exposing the head of the second metatarsal bone.

By September 28, these ulcers were healed without any bone necrosis, and the patient was again discharged with a raised sole on her right shoe and crutches. In November the plantar ulcer reopened. During the next few months the ulcers improved and relapsed, and others developed. The patient was readmitted to the hospital.

July 26.; Typical Pirogoff amputation. All the blood vessels appeared quite normal. Primary union.

Pathological report (amputated foot): The vessels were practically normal, but there was marked bone atrophy. This atrophy was found in portions of the bone remote from the inflammatory process. The nerves of the foot showed no degenerative changes. In the immediate vicinity of the ulcers there were moderate inflammatory changes in the nerves.

¹ Brickner, Am. Jour. Med. Sc., April, 1918, p. 473.

CHAPTER XCI

VASOMOTOR AND TROPHIC DISORDERS IN PERIPHERAL NERVE LESIONS

Some of the symptoms, particularly the trophic disorders associated with peripheral nerve lesions may simulate manifestations attending organic obstruction of the arteries.

The characteristic changes of the integument after nerve lesions are not altogether the sequence of altered circulatory conditions. The effects of exclusion of trophic nerve influences have already been given consideration. Regarding the circulatory derangements some authors describe these as anemia and venous hyperemia. In the former the skin may be pale, dry, and brittle; in the latter, tense, glistening, bluish red or almost cyanotic. These alterations do not seem to depend upon the seat of the nerve injury, but rather are related to fortuitous mechanical factors. Inactivity and atrophy of the musculature play a rôle in influencing the influx of blood. Perhaps the impaired venous return due to deficient muscular action is also an important factor; indeed, this mechanism seems to suffer more than the arterial influx. Although the bearing of direct trophic nerve influences upon the nutritive condition of the peripheral tissues is an important one, many commentators emphasize the preponderating influence of altered or defective circulation as a cause of the trophic lesions.¹

Breslauer, in experimental work on the circulation in extremities whose main nerves had been injured, comes to the following conclusions: That after interruption in continuity of large peripheral nerves or posterior roots the local powers of reaction of the vessels may remain undisturbed in the anesthetic territory for a short period (about 1 week). Subsequently, however, the vascular responses are partly lost. Whilst active vasoconstriction may be conserved, active vasodilatation upon peripheral nerve irritation becomes lost. Superficial anesthesia of the skin and the mucous membrane is associated with diminished vasodilating responses due to inflammatory and other irritants, whilst the vasoconstricting power remains unimpaired.

According to these findings the absence of normal reactive hyperemia would be of great significance as a factor in the causation of trophic disturbances.² The normal integument must adjust itself constantly to the exigencies of external conditions and respond to numerous deleterious influences. As long as the normal physiological vascular reaction is present, active local hyperemia can readily set in, and healing may take place. This means of defense is lost when the vessels in a tissue no longer respond; infection is inadequately combatted, and degeneration of tissues ensues.

The rubor and erythromelia of thrombo-angiitis obliterans and arteriosclerosis may be interpreted as one of Nature's modes of supplementing or counterbalancing local circulatory deficiencies.

After peripheral nerve injury, particularly those injuries due to bullet wounds, two types of manifestations may develop and mimic the symptoms of arterial disease. In the first there are the effects of complete loss of continuity of the peripheral nerves; and in the second irritative phenomena due to partial nerve injury.

¹ Breslauer, *Deutsch. Ztschr. f. Chir.*, 150, p. 51.

² The important rôle of direct nerve influences on the nutritive integrity of the tissues is described elsewhere.

1. Symptoms with Complete Nerve Destruction.—Anesthesia, cyanosis, and pallor may occur and are due to the exclusion of the fibers inhibiting the vascular mechanism. These fibers cross or travel in the peripheral nerves. In addition there may be absence of the excretion of sweat, wrinkling of the skin, hyperkeratosis, loss of hair and stunted growth of the nails. The cyanosis and pallor may give a confusing clinical picture. The anesthesia and trophic disturbances, however, may speak strongly in favor of nerve lesions.

Sciatic Nerve Injury.—When trophic ulcers develop after injury to the sciatic nerve, they do not usually appear until several months have elapsed. Besides the nerve trauma, repeated mechanical excitation of the affected peripheral part is required (rubbing and pressure). Hence the same localization of the ulcerations is observable as in *mal perforant*. Without transverse section of the nerve, the peripheral lesions do not usually follow. The ulcers have little or no tendency to heal spontaneously; they are rebellious to local treatment and persist for months or years without improvement, being complicated from time to time by attacks of local infection. Amputation may eventually become indicated.

Leriche¹ claims that perifemoral sympathectomy (decortication of the artery) in its course through the upper part of Hunter's canal may bring about healing; and that an equally good result may follow resection of a neuroma of the proximal end of the cut sciatic nerve, if such be a complication. Indeed, this author attributes the trophic ulcers of this type to the reflexes engendered in such neuromata. Only temporary healing of the ulcers may follow removal of the neuroma, whilst permanent cures have been observed when nerve resection and repair are done.

2. Irritative Phenomena Attending Partial Nerve Lesions.—The symptom of pain so often noted with the irritative nerve lesions is one that may cause confusion with the intense pain of thrombo-angiitis obliterans. Other associated symptoms, however, would permit of the differential diagnosis.

Neuralgia with or without vasomotor accompanying symptoms is frequently observed after bullet wounds implicating the larger nerves of the extremities.

The pain that follows injuries to both sensory and mixed nerves may be intense if the median nerve and the tibial nerve are involved (Mauss-Krüger²). It may be of great severity and obstinacy with hyperesthesiæ and paraesthesiæ; and usually attended with somewhat less marked vasomotor and trophic disorders. Rubor and swelling are coincidental phenomena, and roughly correspond to the territory of the pain and the paraesthesiæ. The distal parts of the extremities are sites of predilection. The balls of the toes are usually affected in the injuries of the tibial nerve, and also the terminal phalanges of the first three fingers in median nerve lesions. The hypersensitiveness of these parts makes even the slightest tactile impressions unbearable, and renders function impossible.

As the result of the traumatic lesions of nerves, extensive cicatricial strangulation and penetration with connective tissue result, with some endoneural involvement, so that a partial disorganization of the nerve on cross section can be demonstrated. Sometimes the nerve is completely torn, and after cicatrization, although in apparent organic continuity, may be regarded as having suffered complete interruption of functional impulses.

¹ Leriche, Lyon Chirurg., 18, 1921, p. 33.

² Mauss-Krüger, Bruns' Beitr. z. klin. Chir., 1917, 108, p. 163.

The fact that some cases are attended with severe pain, that others with similar lesions do not suffer at all, would arouse the suspicion that causes outside of the cicatricial tissue are responsible. Some authors suggest that there is a general neurotic predisposition, a sort of neurotic component that has to be reckoned with. Given a preformed nervous potentiality, an accentuation of the sensory threshold is brought about through the injury. This suffices, in predisposed individuals, to keep these in a condition of constant hyperexcitability. In this latter state centrifugal impulses that ordinarily do not cause irradiation into sensory territories are intensive enough to arouse the sensation of pain.

Vasomotor and Trophic Symptoms.—Some authors describe the skin as moist, edematous, livid, thinned out and as easily injured. The transverse furrows are obliterated, the integument reddened, parchment like and shiny. Trophic ulcers are to be expected whenever slight traumata, such as burning with cigarettes, pressure of tight shoes or other insults, unwittingly take place. Hypertrichiasis is a striking and important symptom. The nails grow abnormally fast, become friable and distorted, and show transverse ridges. Hyperhidrosis occurs because of the irritation of the sympathetic fibers. Since the secretion of sweat is dependent upon sympathetic and not upon vascular influences, we accept this phenomenon as a symptom characteristic of nerve lesions. It occurs when the nerve lesion is incomplete.

In the descriptions elsewhere given, sensations of cold are mentioned, as also edema, marked cyanosis, blotchy skin and differences in temperature. Even *mal perforant* has been observed. A severe degree of trophic disturbance is usually only present in those cases where considerable interruption in the nerve paths has occurred. Marked trophic disturbances of the foot and leg may attend lesions of the sciatic nerve. Both the intense pain and the neurotrophic manifestations may disappear after successful nerve suture.

Vasomotor Trophic Symptoms Following Bullet Wounds.—Our knowledge of these manifestations has been considerably broadened and clarified by observations made during the Great War on results of bullet wounds involving the peripheral nerves. In a discussion of vasomotor and trophic disorders, the secretory and sensory must also be mentioned, since these may play a part in the symptom-complex. A brief summary of recent observations may be given.

Vasomotor disturbances are exceedingly frequent after nerve lesions, and are most striking after paralysis of the median nerve. In such, the second finger, sometimes the third or the thumb, exhibit violaceous discoloration. In ulnar nerve lesions, the fifth finger—somewhat less frequently the fourth—shows vasomotor signs and cyanosis. With palsy of the radial nerve, there is not the same restricted localization of the circulatory disturbances, but there is cyanosis of the whole of the dorsal aspect of the hand, and of the extensor surfaces of the fingers. Although the pendent position of the hand in the latter palsy may intensify the color, livid discoloration is not due to vascular obstruction.

There seems to be an increased irritability of the vasodilators and a diminished response of the vasoconstrictors. Sometimes as a result of vasoconstrictor irritation, pallor is observed, occasionally a crimson red color. Subjectively the patients complain of coldness of the fingers and hands, and only rarely a prickling feeling of heat.

Trophic disorders are cutaneous changes, particularly atrophy, hypertrophy, ulcer formation, and alterations in the subcutaneous tissue. There

are also changes in the fascia, bones and muscle; even anomalies of hair and nail growth.

In the atrophic type of cutaneous change, the skin is smooth, thin, stretched and tense; it usually accompanies median nerve lesions. The other or hypertrophic type is more often associated with ulnar and sciatic palsy; and the skin is thickened or there is hyperkeratosis.

Important manifestations of trophic disturbances are ulcers, usually small, indolent, and superficial, but that occasionally can penetrate into the depth and cause extensive necrosis. In ulnar lesions the tip of the little finger is usually affected, in median nerve lesions the tips of the second and third; in case of the radial nerve, ulcers are rare. But an area over the dorsum of the first metacarpal may be affected. Usually a slight burn or pressure or a trauma are the exciting factors in the production of the ulcers.

After bullet wounds or other injuries of the nerves the following have been noted: Chronic articular conditions suggesting rheumatism; restricted growth of the phalanges of hands and feet, and bone atrophy. According to Lehmann the following points are characteristic of bone changes after injury to the nerve: (1) Bone atrophy; (2) atrophy whose intensity is in proportion to the degree of neuralgia; (3) atrophy that is not explicable through the degree of inactivity; (4) atrophy localized particularly in the region of the epiphyses and the heads of the bones, the diaphyses remaining unchanged.

Vasomotor Symptoms in Infectious Polyneuritis.¹—In severe cases of polyneuritis following grippe, sensory, vasomotor, and secretory disturbances may be sequelae. Hyperhidrosis with rubor and a turgid condition of the skin of the feet and legs has been reported. During the paralytic stage increased warmth and reddening of the skin of the hands and marked sweating are derangements that are described as running parallel with the motor deficiency symptoms.

CHAPTER XCII

NEUROSES AND THE PERIARTERIAL SYMPATHETIC NERVES

There are clinical complexes in which vasomotor symptoms play but a subsidiary part, and that have been latterly attributed to peripheral, perivascular, sympathetic nerve derangements (French school). A short reference to these may be made here to enable the reader to clearly segregate the so-called true vasomotor from the trophic neuroses.

We must remember that lesions of the peripheral nerves may present manifestations such as paralyses, sensory disturbances, anesthesia, hypo- or hyperesthesia, and pain; whilst lesions of the sympathetic system are said to evoke contractures, circulatory, as well as trophic disturbances.

Observations made during the Great War have emphasized the fact that sensory disturbances may arise from two wholly different sources. For it is now believed that sensory impulses may have their origin in the sympathetic nerves within the realm of the vascular system. The causalgias are regarded as due to lesions in the sensory nerves; a combination of contracture and circulatory phenomena as referable to sympathetic nerve lesions.

¹ Klein, *Wien. Arch. f. inn. Med.*, 1921, II, p. 329.

The Painful Lesions of the Sympathetic.¹—The clinical picture of the sympathetic type of painful lesions is somewhat different. There is usually less pain than in the causalgias. The crises are absent, in that the patient is never so distressed that he fails to take care of his wants, nor does the pain interfere with his sleep. A feature that is characteristic, here, is the presence of contractures. In these there may be flexion of one or more fingers with fixation so intense as to be released neither through passive nor active force. In addition, there are noted circulatory disturbances, bluish or violaceous hands, and trophic disorders. Of the latter, ulcerations of the fingers may be mentioned. The radial pulse may be absent and there often is a history of ligation of the brachial artery.

Combinations of irritative lesions of the sympathetic and lesions of the peripheral nerves may occur, usually with involvement of the median nerve that courses in the immediate neighborhood of the sheath of the brachial artery. In such cases the circulatory disturbances are localized in the cutaneous territory of the median nerve in the form of violaceous discoloration of the hands, the territory of the ulnar and radial showing no such discoloration.

As an example of contractures and circulatory disturbances, possibly of this type, the reader is referred to the second example of embolic closure of the brachial artery (Chap. LXXXV, p. 496). Here, it is true, there was an infection after an embolectomy or removal of a clot and the contiguous nerves may have been implicated. It was in this way that the neurologists interpreted the vascular and contracture phenomena. Nevertheless the clinical picture resembles rather those complexes which the French authors describe as caused by disorders of the periarterial sympathetic.

The Sympathetic Nerves in Relation to Causalgia.—Causalgia (a complex associated with peripheral nerve lesions) includes painful syndromes of focal types. Amongst the symptoms are constant pain, burning sensation, paroxysmal crises of pain evoked by the slightest touch of the part with an external object, or with something that is warm and dry. Only objects that are wet and cold ameliorate to a slight extent the acuity of the symptoms. In some cases all the usual physiologic acts, even the idea of performance, may provoke paroxysms of intolerable pain.

In addition to the sensory symptoms there may be absolute functional impotence, but of such character that differentiation between actual paralysis and fear of execution of motion is difficult.

Of some interest was the observation of Leriche² that certain extremely rebellious cases of causalgia, upon which no effect had been produced by division of the nerve in question, were at least temporarily cured by stripping the sympathetic fibers from the blood vessels below the nerve lesion. He concluded therefrom that the exciting cause of the manifestations was not a lesion of the nerve itself, but of the neighboring perivascular sympathetic.

Causalgia according to certain French authors³ is essentially a sympathetic symptom-complex, in which through a sympathetic reflex arc, there occur painful centripetal excitation and centrifugal reactions of the vasomotor form, and secretory or neurotrophic disturbances. These aid in prolonging and augmenting the pain. When the lesion of the nerve implicates sympathetic fibers, the point of departure of the painful sympathetic excitation can be anatomically found. In such a case relief from pain may be obtained by section of the nerve above the lesion. Where, despite this procedure, the

¹ These views of lesions of the French school must not be accepted as final.

² Leriche, *Presse méd.*, 1917, 25, p. 513.

³ Tinel, *Rev. Neurol.*, 1917, 243.

causalgia persists, it is assumed that there exists an irritation of the sympathetic terminations in the peripheral territory of the nerve. In such cases the painful sympathetic excitations, like the reflex responses, are conducted by the lateral, probably *perivascular* paths. These painful excitations induce a state of marked hyperexcitability in the sympathetic, diffusing into the neighboring centers, and even into the homologous centers of the opposite side. This condition (described as *erythema*) is accompanied by "synesthesalgia," which is not infrequently restricted to the clinical "causalgic field." Modifications in sensibility, especially a superficial hypesthesia by inhibition or even blocking of the sympathetic, may be observed in quite a large sympathetic field. Profuse sweating, mydriasis and vasodilatation, evidences of diffuse sympathetic reaction, are noted in distant parts.

For the sympathetic origin of causalgia, the French school adduce confirmatory evidence.¹ Contractures have been observed as the dominant findings in painful affections of the limbs, and with these, lesions of the periarterial sympathetic were repeatedly encountered. In these periarterial sympathectomy is said to have afforded relief.

Without reflecting on the correctness of the therapeutic results obtained after the operation of periarterial sympathectomy or decortication, it is noteworthy that anatomical and physiological facts do not offer a satisfactory explanation for these. Leriche assumes—and the rationale of his procedure is perhaps based thereupon—that the majority or all of the vasomotor fibers course in the sheaths of the larger arteries in uninterrupted paths. It has been elsewhere shown that this is not the case. The effect of the operation could not altogether be due to an interruption in the continuity of these fibers. Perhaps reflexes engendered, however, may be responsible for some of the consequent alterations of innervation.

Treatment.—Three types of treatment are applicable for these diverse clinical complexes. On the one hand, for relief of the causalgias, the nerves involved—such as the median, sciatic, popliteal—require our attention. Interference with the conduction of pain impulses to the higher centers may give relief. Intramural injections of alcohol, or injection of other substances such as novocain and saline solutions, have been suggested.

In the irritative manifestations of the sympathetic type Leriche has suggested periarterial sympathectomy. Finally, electrotherapy and physiotherapy of various forms are valuable adjuvants.

CHAPTER XCIII

TRAUMATIC VASOMOTOR SPASM

Clinical observations made during the Great War have emphasized the importance of recognizing the occurrence of local vascular spasm of traumatic nature. It had already been noted by the author in 1910-1911, and by numerous observers since, that exposure of an artery, such as the radial, for purposes of direct transfusion was frequently followed by such intensive spasm that no blood would flow through it. Similar arterial spasms may develop when wounds are inflicted in the vicinity of large vessels. Such

¹ Girou, *Presse méd.*, 1918, LXIII, 584.

vessels on excision may be found completely patent, even though pulsations had been absent.

The following observation of Küttner and Baruch¹ is a typical one.

A soldier (Aug., 1916) received a number of injuries from a hand grenade. On the outer side of the Achilles tendon of one leg there was an irregular bullet wound of entry, immediately above the heel. There was no arterial bleeding, although venous blood oozed from the wound.

Operation was done 4 hours after the injury, and the wound of entry and exit were excised. The Achilles tendon and bone were found intact. The posterior tibial vessels were exposed after excision of the bullet tract. The posterior tibial vein was torn and the injured portion resected and vein ligated. The *posterior tibial artery was found uninjured*, although there was some inhibition of the adventitia with blood where it was in contact with the vein. *Pulsation in this part of the artery was absent.* On dissection of the artery it was found that pulsation was strong above, whilst towards the periphery all pulsatile excursions were absent.

The diagnosis of thrombosis was made. About $2\frac{1}{2}$ cm. of the non-pulsating portion of the artery was removed, and ligation done. Immediately upon *resection of this region, the peripheral portion began to pulsate.*

Examination of the artery showed that thrombosis was absent, the intima was intact and the vascular wall normal.

Küttner and Baruch report 23 cases of traumatic vessel spasm. Other cases are reported by Abadie, Delbet, Fiolle, Leriche and Tuffier.

The clinical course and the causal mechanism in these cases have been illuminated by the recognition of a special morbid syndrome. This comprises more or less complete interruption of the circulation of a member through traumatic irritation of the region of the supplying artery, usually unattended with organic arterial alterations of any significance.

In the severe cases gangrene may occur. The peripheral pulses are absent and the affected extremity is cold and blanched, having a yellowish or slightly bluish tint. There are sensory disturbances, either absent or diminished, and active motility is impossible or motion is carried out with great difficulty. When this condition lasts for many hours, the outcome in gangrene is so certain, that some of the authors have recommended early amputation.

Leriche² reports cases in which the arm was limp and lifeless, and the fingers colorless so as to give the impression "that the brachial artery was crushed." In these the manifestations were of temporary nature.

Although threatening gangrene is occasionally observed, no case of absolutely authoritative example of true gangrene following protracted spasm of arteries (traumatic) can be found in the literature. There are 5 cases (Küttner, Baruch) in which gangrene was expected, but in which restitution occurred even though threatening symptoms were present from 4 to 12 hours.

In cases of moderate severity, the only striking sign may be an absence of peripheral pulse, suggesting the diagnosis of a solution of continuity in the supplying artery.

In the mild cases we may group those in which the peripheral pulses are still present, although diminished. The qualitative differences may be such as to require the use of a blood pressure apparatus for differentiation.

Another symptom referable to vasoconstriction is an unusual sort of burning pain. It may persist for months or even a year, may be continuous or return in paroxysmal crises together with painful hyperesthesiæ.

Pathogenesis.—The characteristic pathologic change in 20 cases was the constriction of the affected arteries. Although it must be admitted that

¹ Küttner and Baruch, Brun's Beitr. z. klin. Chir., 120, p. 1.

² Leriche, Ann. Surg., LXXIV, 1920, p. 388.

similar observations on small arteries might be inaccurate, it is the large arteries that are usually affected (common carotid, brachial artery, posterior tibial). The spasm usually is localized over an area of from 2-5 or 10 cm. in length. The transition from the narrowed to the normal portion is a sudden one, where the delimitation is evidenced by a narrowed zone. The pulse wave encounters here a more or less insurmountable obstruction, so that the artery beyond the ring of spasm is pulseless and motionless. Only in one case where operative demonstration of this phenomenon was reported was a peripheral pulse palpable.

Three cases are reported in which the exsected and opened artery was absolutely normal, the intima being intact, the adventitia presenting merely localized hemorrhagic infiltration. It has been conclusively proven that this spasm can occur without anatomic lesion of the arterial wall.

In short, the gross anatomic changes do not throw any light upon the pathogenesis of this type of morbid entity.

A number of explanations have been given for the causative factors in traumatic vascular spasms. Vascular contraction is explicable either through irritation of the vasoconstrictor nerves of the sympathetic, or through direct irritation of the vessel's musculature. According to some, the mechanism that conserves the vascular tone lies in the vessel wall itself, and is merely regulated by the central vegetative nervous system. These believe, too, that an autonomic nerve mechanism, such as exists in the heart, can be attributed also to the vessels.

Küttner and Baruch, in the consideration of traumatic vascular spasms, lean to the view that the theory of myogenic origin can best explain the occurrence of localized vessel spasm of traumatic type. It is well known that most vessels react intensively to mechanical external stimuli. Thus, sudden changes in temperature cause vasoconstriction in vessels that have been robbed of their nerves. The manipulation incident upon the dissection of vessels for purposes of transfusion has demonstrated, too, that mechanical irritation produces local vascular constriction.

It must be admitted that we have no absolute means of differentiating between the symptoms of impaired circulation due to local vasoconstriction, and mechanical interference with the patency of vessels.

Prognosis.—As a rule, the outcome is good. However, because of the uncertainty, and the threatening nature of the symptoms, intervention with resection of the affected vessel has been frequently resorted to and deemed advisable.

Therapy.—Resection, although done in some of the cases reported in the literature, should not be regarded as a correct procedure, since the absence of pulsation in a part of a vessel under observation does not necessarily imply a persistence of the phenomena. Some authors recommend irrigation with hot saline solution, others massage of the constricted portion of the vessel. The subcutaneous injection of atropin should be tried.

Decortication and Peri-arterial Sympathectomy.—Leriche¹ reported interesting results after interrupting the sympathetic pathway in arteries of the limbs by decorticating the vessel for a distance of about 8 to 10 cm. Horrax states that two distinct reactions followed such procedure, one, lasting for 6 to 12 hours, consisted in a contraction of the artery to one-quarter of its former volume over the decorticated area, feeble or imperceptible pulse in the extremity, and a lowering of the surface temperature of the limb. The other reaction, lasting for 2 weeks to a month, consisted in an elevation of 2 to 3 degrees of the surface temperature of the limb. This procedure has also been recommended, although insufficient data are yet at hand to give it a definite recognized value as a therapeutic agent.

¹ Leriche, Soc. mèd. des hôpitaux de Lyon, Dec. 2, 1919; Lyon, méd., Jan. 10, 1920, 40.

CHAPTER XCIV

LOCAL SHOCK

Local shock is an appellation given to certain vasomotor and sensory phenomena caused in an extremity by trauma. Since there are marked vasomotor disturbances with noticeable changes in the pulses of the affected limbs, a knowledge of this symptom-complex belongs to the domain of the morbid conditions discussed in this treatise.

Characteristic manifestations are local derangements of motility, sensibility and circulation—these being evidences of a local depressive state. Such a condition is said to result from local shock of the peripheral nerves, although this explanation is not altogether convincing. According to Seydel,¹ a bullet tract and its surrounding parts may be found insensitive. Or, this condition may spread over a larger territory so as to implicate the whole or a large part of the limb, or corresponding section of the body. v. Mosettig describes the limb affected as being cold, its skin pale or bluish, the part paralyzed and without sensation. Indeed, patients may have the impression that the part is absent, having no sensation therein. At times there are formication and other paresthesiæ.

Wieting² observed cases with somewhat different symptomatology during the Great War. In these, after severe exposure or after intensive contusion of one or both lower extremities, striking manifestations were noted. Besides the immediate results of the trauma, which was in no case an open wound, the limbs were found *immobile and pulseless*. With this there were the symptoms of severe shock except for a relatively slight acceleration of the pulse. Within 48 hours or in a very few days, death ensued. At autopsy the internal organs were found normal. It is true that the muscles of the contused extremities were extensively lacerated, showing degeneration and white and hemorrhagic foci. Possibly autolytic tissue changes and resorption of toxic substances were factors in the clinical manifestations. Some of the cases recovered.

Pathogenesis.—A reflex nerve mechanism through the spinal cord is regarded as being at play in *local shock*. The insult probably stimulates the peripheral nerves throughout. Impulses from the whole cross section of the limb are then transmitted to the spinal cord by way of the sensory nerves, and sympathetic cord. Granted that a “shocked” condition of the reflex arc may be produced by trauma, then a paralytic vasomotor effect must needs occur. There is never isolated participation of single nerves, even of considerable size; but all of the nerves at the injured level are involved.

The gradual transition of local to generalized shock, however, is a phenomenon that has not been adequately explained. How does a local vessel palsy become ubiquitous after abatement of the exciting traumatic cause?

Diagnosis.—The early local signs of gas bacillus infection when deep seated may be mistaken for local shock, all the more so since the limbs, already in the condition of local shock, were found especially prone to this type of bacterial invader.

Immediate injury of peripheral nerves, or lesion of such without anatomical alteration, must be excluded. Characteristic for the latter is the

¹ Seydel, Lehrbuch d. Kriegschirurgie.

² Wieting, Ergebn. d. Chir. u. Orth., 1921, 14, p. 656.

fact that the symptoms are confined to the territory supplied by the affected paths, whilst in so-called local shock, the territory involved extends from its inception at and about the wound or traumatized zone, in every direction until the whole limb is implicated.

Critical Observations.—The remarkable sequence of local shock giving way to generalized shock with frequent lethal outcome would tend to substantiate the toxic theory of shock; namely, that certain forms of the latter are due to the action of toxins arising in injured tissue. This view is further upheld by the following observations: that removal of the injured region may cause the symptoms of shock to disappear;¹ and that the application of a tourniquet as tightly as [possible around a limb that was so badly contused that amputation seemed unavoidable, was followed by immediate improvement (McNee, Sladden and McCartney²).

These together with similar observations offer a suggestion as to treatment in local shock, wherever severe and irretrievable damage of an extremity has been sustained.

CHAPTER XCV

CHRONIC ACROASPHYXIA

This is a clinical syndrome to which some of the Continental authors have called attention—a clinical complex of neurogenic variety, that may easily be confused with some of the forms of organic vascular disease of the extremities.

Characteristic of acroasphyxia chronica is the slow development of cyanosis or asphyxia of the terminal portion of the extremities. These manifestations are not unlike those attending Raynaud's disease. There is, however, this difference, that *paroxysmal attacks are absent*. Associated with this manifestation there are other symptoms of trophic and sensory nature. Or there may also be present a neuropathic diathesis or other nerve malady.

Cassirer was the first to group these cases under the caption "Chronic Acroasphyxia." Whether all the cases previously described with their manifold deviations are correctly classed as an entity under this appellation, and just what their relationship to Raynaud's disease is, has not yet been satisfactorily answered.

In one of the usual forms there is acrocyanosis unassociated with pulmonary or cardiac disease, the discoloration developing rather suddenly over a period of a day or several weeks. A peculiar hypesthesia seems characteristic. The sensory symptoms do not appear to be of hysterical nature, although evidences of a general neurotic habitus are present.

The following brief history is rather typical of the disease.³

A young woman of 19 years gave a history of tendency to frost-bite and to the development of painful fissures. Two weeks ago the hands began to be discolored, dark bluish red, there being sensation of prickling in the affected parts. Pallor or blanching was absent, the

¹ Cannon, Arch. Surg., 1922, 4, p. 1-22.

² Cited by Cannon.

³ Cassirer, Vasomot. trophisch. Neurosen, Berlin, 1912.

discoloration taking on a progressively darker hue. Pain, too, was absent, but a feeling of lack of sensation attended with prickling and tingling was experienced. Amongst the more remote symptoms were headaches, increasing nervousness with exaggerated sense of fear.

Examination showed bluish red discoloration of the distal portion of both hands. The fingers were dark red throughout, with a bluish tint over the dorsal part of the hand extending almost midway up to the wrist. Hyperhidrosis was distinct, the hands being cold to the touch, this coldness extending up to the forearm. Except for old scars and fissures, the skin of the hands was negative. The feet also showed a certain degree of cyanosis, but to a less marked degree. The cyanosis of the upper extremities was roughly symmetrical, there being a slight difference in the intensity of the discoloration. Associated with these symptoms was a distinct diminution in the sensibility over the affected parts. All of the sensory qualities were involved. The limits of the hypesthesia could be distinctly demarcated in a line roughly perpendicular to the long axis of the limb.

This condition lasted for months, the coldness and cyanosis persisting even in a warm room. On immersion of the hands in cold water, the bluish color became much darker. Local syncope was noted at no time. Pain was absent, and the paresthesiæ were of but slight degree.

The feature of this clinical picture is the bilateral peripheral acrocyanosis of both hands, developing rather rapidly within two weeks. The hypesthesia, neurotic symptoms, and a susceptibility to chilblains are also noteworthy. To this type the name, "*acrocyanosis chronica anaesthetica*," has been applied.

If we compare this affection with Raynaud's disease which it resembles most, we find the same localization, but the absence of syncope. This alone would not sufficiently differentiate it from Raynaud's disease, since even blanching may be absent in the latter malady. However, *the absence of pain*, as well as of the paroxysmal attacks and the progressive development of cyanosis, are real distinguishing criteria. Indeed, paroxysmal attacks are pathognomonic of Raynaud's disease. The anesthesia of this type of acrocyanosis is also rather suggestive, for it is rare in the Raynaud complex.

Another interesting observation of this nature is reported by Barker and Sladen.¹ The history may be summarized as follows:

A male, 44 years of age, began some 10 years previously with the present condition, the onset being characterized by cramp-like pain in the leg that would come and go. This, however, disappeared after 5 years. Then there occurred multiple attacks of numbness of the fingers without discoloration. Subsequently and gradually came a feeling of numbness in the toes of the feet, and latterly, a bluish red discoloration with nutritional disorders of the skin and nails developed, but unattended with any painful sensation.

Physical Examination.—Both feet and part of the legs were cyanotic; the pedal arteries pulsated; the first three toes of the right foot showed ulcerations; and there was a large ulcer over the plantar aspect of the big toe. There was also cyanosis of the hands up to the wrist.

In short, 6 weeks after the first observations were made, the picture was as follows: marked cyanosis of the right foot, less of the left; the hands cold and cyanotic without syncope even after dipping into cold water; all the arterial pulses present, the trophic disorders disappearing after removal of the distal phalanges of the first and second toes (right).

The authors summarized this case as characterized by (1) cyanosis and swelling of the soft parts; (2) paresthesia and anesthesia that do not correspond to the distribution of any nerve; (3) absence of pain; (4) dystrophic disturbances in the skin and bones, localized to the fingers, toes, feet and lower extremities; and (5) with a chronic progressive, and not a paroxysmal course.

Acroasphyxia Hypertrophica with Marked Trophic Changes.—A certain group of cases, in which besides the asphyxia there are distinct trophic disorders of the soft parts, have been classified under this caption. The clinical picture has a certain resemblance to acromegaly. One of Cassirer's cases will illustrate:

¹ Barker and Sladen, Jour. Nerv. and Ment. Dis., 1907, p. 745.

A male 42 years of age had been well until 1904, when, after a fall, he passed into a stage of chronic suppuration lasting some years. In the course of the next year and a half he had a number of foci of osteomyelitis. Then there came the gradual changes in the hands and feet. It is of these that he complained when the history was:

The color of the hands gradually became more and more blue *without* attacks of syncope, and the hands also became awkward. Enlargement of the hands then took place, so that he could find no glove to fit him. Because of the coldness of the hands, gloves were necessary and these had to be made to order. The sensibility of the hands too diminished, particularly to warmth, hot water. *There was no pain at any time.*

Later his feet also showed similar, but less pronounced, changes. No alterations were noted in the face.

Physical Examination.—A powerful man with normal organs. The hands are totally discolored, bluish with isolated red and cyanotic patches. The color change reaches intensively up to the wrist, and from there on in diminished tints up to the lower limit of the middle third of the arm. The temperature of the skin is diminished irregularly; the hands markedly enlarged, plump. The dorsal and solar aspects look padded, the skin being devoid of induration. The latter is rather soft and succulent. The fingers are sausage-like by reason of their enlargement, the distal phalanx about as thick as the first.

All the arteries of the hands and legs pulsate normally, including the brachial and femoral arteries. There are no changes in the motility and electric reaction. Sensory disturbances are demonstrable especially in the diminution of the temperature sense. In the roentgenogram the bones are intact, the enlargement being limited to the soft parts. No evidences of acromegaly are present.

Other instances have been reported, in which acromegaly is said to be associated with an atypical Raynaud complex. When the usual symptoms of acromegaly are absent, they belong more properly in the class of chronic acroasphyxia hypertrophica. In a number of such cases, the following characteristic symptoms of acromegaly were absent, namely, headaches, enlargement of the lower jaw, visual disturbances and kyphosis. In acroasphyxia the bones are not essentially implicated, and the vasomotor disturbances may precede the trophic alterations by a considerable period of time.

The Mild Form.—In the less intensive form, this affection is more frequently observed. There may not be any parallelism between the intensity of the vasomotor and trophic derangement. The latter are more apt to be minimal or almost absent.

In a case of Oppenheim, a woman 31 years of age, the fingers of both hands were deep reddish blue, the hands less cyanotic. The skin of the fingers was smooth and soft, with no indication of sclerodactyly. The sensibility was intact, the nails without change.

In the above instance in spite of a rather long duration (13 years), the nutritional changes in the hands were very slight, although there had been permanent asphyxia for a long time.

More frequently the acroasphyxia is associated with but very slight enlargement of the terminal phalanges without osseous changes, the subcutaneous connective and fatty tissues only being involved. The hands are diffusely red and cyanotic, cold and somewhat moist. They may seem large and extraordinarily soft. The compression test or circulatory return in the skin demonstrates rapid reflux.

Such cases are not uncommon, and have been explained as due to thyroid malfunction.

Acroasphyxia and Acromegaly.—These have been reported as not infrequently associated in several cases. Even a symptom-complex (Oeconomakis¹) in which acroasphyxia, acromegaly and gigantism are combined has been described. Chvostek and Bonardi cite similar combinations. Chronic local asphyxia in such cases is believed to be due to malfunction of

¹ Oeconomakis, Neurol. Centralbl., 1917, 36, p. 578.

the hypophysis, either by virtue of direct action or through the nerve centers. The possibility of diffuse glia hypertrophy in the central portion of the vasomotor apparatus had been suggested by Cassirer as a possible cause, as a parallel hyperplasia of neuroglia tissue has been believed to exist elsewhere in the nervous system in acromegaly.

The hypertrophic changes do not seem to be dependent upon the vasomotor, since they may precede or appear simultaneously. Oeconomakis assumes that in this case (one of *acroasphyxia chronica anæsthetica*), there was a combination of *acroasphyxia chronica anæsthetica* and acromegaly, and that furthermore the manifestations could be referred to a proliferation of glia tissue in the central vasomotor apparatus.

Acromegaly and Gigantism.—A man of 21 years of age developed dull pain 5 years before observation, prickling sensation at the tips of the hands and feet, then also at the tip of the nose and ears, this soon followed by a purplish or dark violaceous discoloration. Within 3 weeks the present condition of complete and persisting cyanosis had been brought forth. Simultaneous with the appearance of the cyanosis there was a progressive enlargement of the hands, the pain and paresthesiæ disappeared, but the cyanosis and enlargement remained. Associated with the asphyxia was a corresponding diminution of sensation to touch, pain and temperature; in short, the symptoms of *acroasphyxia chronica hypertrophica*.

As for the signs of gigantism, these were evolved simultaneously with the cyanotic discoloration. Not only did the hands become larger, but a generalized increase in size was noted. The osseous changes were a general dystrophy with destructive and atrophic changes, particularly of the feet and the terminal phalanges of the toes. The broadening of the maxillary and frontal sinuses, unusual enlargement of the occipital protuberance, and an irregular thickening of the cranium, were some of the manifestations and signs of acromegaly.

Diagnosis.—1. *Acrocyanosis chronica anæsthetica* is not easily confused with Raynaud's disease. The two maladies are similar in the localization and the type of cyanosis. The intensity of the pain, the absence of paroxysms, and the gradual development of the cyanosis are characteristic for *acroasphyxia*. Anesthesia, too, is but rarely encountered in Raynaud's.

The sensory disturbances may simulate those of syringomyelia, but the complete absence of motor and trophic disturbances distinguishes it from that affection.

From vasomotor phenomena polyneuritis it differs in that sensory, irritative phenomena are absent, also motor, irritative and paralytic manifestations.

2. *In the chronic hypertrophic form*, the chronic progressive course of asphyxia, and the gradual increasing volume of the parts are characteristic. Only the less pronounced cases may be confused with Raynaud's disease. Differentiation must be based upon the following points: the absence of gangrene, the minimal intensity of pain, the absence or rare appearance of local syncope, the permanency of the cyanosis and increased volume of the parts. All of these speak for chronic asphyxia and against Raynaud's disease. The extent of the cyanosis is especially noteworthy in that the hands are most intensively involved, the color change is permanent, involving the forearm to its middle or higher. The diminished temperature of the hand and the hyperhidrosis are other peculiarities. In contradistinction to the Raynaud syndrome the end phalanges are either negative or show distinct enlargement. The skin is not indurated but is softer than normal, is not adherent to the deeper tissues, and, by reason of its succulent appearance, is not unlike that often attending syringomyelia.

These cases must also be distinguished from the chronic cyanoses that accompany the hypertrophic osteopathy of pulmonary type, and furthermore from the polycythémias with enlargement of the spleen.

3. *The mild chronic forms* of acrocyanosis may escape observation because of the paucity and slightness of the manifestations. Atrophic forms must be carefully differentiated from scleroderma. These cases are very rare.

4. *Differentiation from Organic Vascular Diseases.*—If we keep in mind the symmetrical nature of this affection, and the diffuse cyanosis, and if we remember the association of anesthesia with or without hypertrophy in other forms, the recognition of the malady will not be difficult. The two atypical varieties, that with atrophy and the mild form with cyanosis alone, may give rise to greater difficulties of recognition.¹

5. The early vasomotor manifestations of *thrombo-angiitis obliterans* may be confounded with this affection at a time when all the usual vessels are found to pulsate. A typical case of thrombo-angiitis with cyanosis as a feature has been described elsewhere. In the latter the cyanosis may be restricted to the toes, not so frequently extending over the greater part of the foot; is not symmetrical and is usually associated with pain that becomes more and more intense with the degree of cyanosis. The asphyxia in thrombo-angiitis obliterans is not permanent until the stage of threatening gangrene is at hand. Then, restricted in extent and intensity to but a part of the foot or hands (usually toes or fingers) it is soon followed by trophic disorders or gangrene. Ischemia and rubor may be absent at this stage, and a considerable period may elapse before we can be absolutely assured of the organic nature of the malady. Nevertheless, the features already alluded to are characteristic enough to permit of differentiation.

6. In the *peripheral vascular thromboses*, with or without atherosclerotic changes in the artery, acrocyanosis is usually limited to one or several toes, and is also not symmetrical, although both lower extremities may be involved at different times (p. 490).

7. An *asphyctic* type of vasoneurosis usually confined to a toe, may be a manifestation complicating arteriosclerosis; it does not properly belong here (see p. 578).

CHAPTER XCVI

ERYTHROMELALGIA

Weir-Mitchell in 1878 described an affection characterized by the paroxysmal occurrence of *pain, redness* and *swelling* of the feet, under the designation "erythromelalgia." *Hyperesthesia*, motor, secretory and trophic disturbances may amplify the syndrome.

1. *The Pain.*—The predominant symptom is a burning and sticking *pain* that may attain unusual intensity, oftentimes likened to the effect of "fire in the skin," arising either suddenly with great severity, or gradually increasing from paresthesia up to a maximum degree. Thus from a feeling of prickling, formication, or numbness, pain seems to loom up augmenting until unbearable tortures that prevent sleep are oft experienced.

Three factors influence the pain, the *pendent* position of the foot, *heat* and *exertion*. Considerable diminution of the pain is brought about by raising the feet to the horizontal and keeping them at rest.

The *onset* of the pain is described by Weir-Mitchell as in the foot, in the sole, or in the big toe, at times extending over the dorsum so as to involve

¹ Chap. CIV.

more or less of the leg. Cassirer gives the following figures as to localization of pain: in both feet twenty-four times, in one foot nine, in both hands thirteen, in one hand four, and in all four extremities, seventeen times. In the foot it is the toes, heel and sole; in the hands it is the fingers that are the sites of predilection for sensory disturbances.

2 and 3. *The Redness and Swelling*.—Rubor may not appear simultaneously with the pain but subsequently, for a period of sensory disturbances may antedate the advent of the discoloration by weeks or even months. At times redness, pain and swelling are coincidental in their onset. The color seems to be due to an active hyperemia, is a bright red, varying to a purplish hue attended with strong, bounding pulsations of the arteries and dilatation of the veins. Weir-Mitchell states that the active hyperemia yields to a passive stage, the arterial beating seems to abate, the bright red color changes to bluish red or violet with distinct manifestations of impaired oxygenation of the blood. Thus a variegated succession of colors from a bright red to a livid blue may be seen.

The rubor is confined to the painful zones, usually the distal portions of the extremities, and the color returns rapidly after being made to disappear by digital compression.

Accompanying this phenomenon there is often *swelling of the skin* that is transitory and evoked by the overfilling of the vessels. The temperature of the skin, too, is increased as has been demonstrated by actual thermometric measurements.

As for the duration, this combination of symptoms is prone to come on in attacks that are incited by pendency of the feet, by heat or by exertion. We may distinguish two types, the *recent* and *old* cases.

In the *recent* cases there are ordinarily no disturbances in the horizontal posture, but they appear immediately on allowing the limb to hang down. The local temperature rises, the arteries pulsate strongly, and the rubor becomes intense.

The *old cases*, on the other hand, differ in that redness and pain are apt to persist in the horizontal position whilst the heightening of temperature with pendency is missing.

The *extent of the rubor* corresponds within a somewhat restricted area to the seat of the pain, either delimited by a sharp boundary, or diffusely fading out into the normal. It is not exactly symmetrical since many variations and irregularities both in intensity and distribution are noted. Although it is the rule to find the so-called "acra" or peripheral ends of the distal parts attacked, cases in which a typical localization occurs are not infrequent, as in the elbows, knees, and forearm, without implication of fingers or toes.

4. *Hyperesthesia* of the affected areas especially to touch is a fairly constant manifestation, the patients being unable to endure the slightest pressure on the affected parts, even the weight of the bed covers being unbearable. They are frequently unable to wear stockings and shoes, and even the milder cases must walk with the greatest care, bearing their weight on the uninvolved parts.

5. *Associated symptoms* may be classified as:

- | | |
|-----------------------------|---------------------------|
| (a) Secretory disturbances. | (c) Sensory disturbances. |
| (b) Trophic disturbances. | (d) Motor disturbances. |

(a) *Secretory disturbances* in the form of hyperhidrosis are not uncommon, over the palms, and soles of the feet, and, in general, corresponding in site to the rubor and pain. Profuse local perspiration coincidental with attacks of pain is a phenomenon reported by Weir-Mitchell and others.

(b) *Trophic Lesions*.—These are said to occur in somewhat less than one-third of the cases. Thus, (1) *blebs* of lentil or split-pea size on a reddened base that heal, giving way to others in various situations; or desquamation of the skin of the ball of the thumb following bullae formation; (2) *thickening* of the skin not due to edema but to vascular dilatation and possibly connective tissue proliferation; (3) *atrophy* of the skin, the latter being smooth and fissured over an apparently enlarged phalanx, or parchment-like; (4) *dystrophies* of the nails and hair; and (5) rarely, in the late periods of the disease, *gangrene*¹ is a possible concomitant. This in its extent resembles that of Raynaud's disease. Only very seldom has an early association of the trophic with the vasomotor signs been noted, *so that a sufficiently long period is usually at hand in which the true nature of the disease may be recognized*.

(c) *Sensory Disturbances*.—The pain and sensitiveness to tactile irritants have been discussed above. Anesthesia and various degrees of hypæsthesia have been occasionally reported.

(d) *Local motor disorders* such as paralysis with atrophy and reactions of degeneration in the territory of one or more nerves are absent. Simultaneous motor, sensory and vasomotor phenomena, however, have been observed when there is marked muscular atrophy. Weakness of the hands to the extent of an almost total loss of functional activity is cited by Weir-Mitchell.

Other Coexisting Maladies.—As complicating the symptom-complex here described, it cannot be denied that other diseases, particularly of the nervous system, both functional and organic, may be coincidental. Cardiac affections, myxedema and osteomalacia also have been reported.

Frequently a neuropathic habitus may be associated. Amongst the manifestations of the latter may be mentioned nocturnal emotional states, restlessness, attacks of vertigo, headaches, insomnia and nervous dyspepsia.

Psychoneuroses too, melancholic states, and others are occasionally synchronous or prodromal morbid manifestations.

Organic nerve diseases, such as antecedent cerebral hemiplegia, with symptoms on the paralyzed side, cerebral lues, paresis, tabes dorsalis, multiple sclerosis, and myelitis have been known to occur with erythromelalgia.

In some instances, the symptoms seem to be restricted to the territory of one or more nerves *without the presence of neuritic manifestations*. Morgan reports a median nerve distribution; Weir-Mitchell, the posterior tibial; Oppenheim, the ulnar, and a number of other authors still different localizations.

Pathogenesis.—As to whether erythromelalgia should be regarded merely as a symptom-complex associated with a number of diseases, or as to whether it deserves to be dignified into a morbid entity, is still a mooted question. Certain it is that similar manifestations, such as accompany obstructive arterial disease, when carefully studied will be found to present so many discrepancies from the Weir-Mitchell type as to require small powers of observation for differentiation.

Two distinct types of erythromelalgia exist:

1. That in which the local symptoms follow the paths of certain nerves and
2. That in which diffuse dissemination over certain peripheral parts occurs.

Cassirer gives the following pathologic basis for these two forms: In the *first group*, we may assume an irritative process in the peripheral nerves with especial predilection for the *vaso-dilator* and *secretory* fibers, the sensory

¹ Bikeles, Wien. klin. Wchnschr., 1915, 30, p. 816.

also being involved. However, the disparity between the true neuralgias and neuritides is adequate to justify a separation of erythromelalgia into a separate clinical entity.

In the *second group*, the existence of a central nerve origin is a warranted assumption, the vasomotor, secretory and sensory elements being implicated. The sympathetic system is in all probability the seat of the disease.

Clinical Course.—In the majority of cases a chronic progressive course is observed, more rarely the onset is sudden. The manifestations may remain stationary after having attained a certain degree of intensity and extent of distribution, or may even recede gradually. Quite a number of cases of improvement after several years' duration are on record and in a few instances even cure after months or several years of manifestations. In general, a noteworthy degree of obstinacy is characteristic when the phenomena have become marked.

The *prognosis* is therefore extremely dubious, complete cure being rare, improvement infrequent after months or years have elapsed. *Quo ad vitam* there is no danger from the disease, the lethal cases being those complicated by organic, cerebral, spinal, or cardiovascular affections.

*Diagnosis.*¹—For the clinical diagnosis the two striking phenomena of *rubor* and *pain* are essential. However, it must be remembered that mere hyperemia in a limb that is painful or becomes increasingly painful when pendent is not a complex upon which the diagnosis of erythromelalgia should be made, for this association of rubor and pain is an almost pathognomonic feature of thrombo-angiitis obliterans, and may even attend arteriosclerotic vascular occlusion in certain stages of the affection. So we must separate what some have called a *symptomatic complex* similar to erythromelalgia from the *essential, intrinsic form* or true erythromelalgia. The former may accompany a number of other maladies and be not at all of vasomotor origin.

The syndrome to be sought for in true erythromelalgia is a combination of:

Active hyperemia, with the typical rubor, swelling and severe pain, occasionally also secretory and trophic derangements of paroxysmal appearance characteristically localized in the distal portions of the extremities.

From *thrombo-angiitis obliterans*, differentiation should be easy if the peculiar features of the disease be comprehended. We may tabulate a comparative review of the two affections thus:

Thrombo-angiitis

Arteries obliterated, do not pulsate.

Rubor constantly present also intensified in pendent position; it disappears completely yielding to ischemia on elevation. The redness disappears on digital compression, color returns sluggishly.

Pain often intensified in pendent or elevated position.

Swelling usually absent; in some, peculiar chronic puffiness that does not disappear.

Erythromelalgia

Arterial pulsation bounding, stronger during the attack.

Rubor paroxysmal, *intense in pendent position*. On digital pressure disappearance, but *rapid* return of the color. Ischemia not demonstrable.

Pain in attacks brought on by posture, intense, often unbearable.

Swelling temporary associated and induced by posture.

¹ For the application of Capillary Microscopy in differential diagnosis, the reader is referred to Chap. CVI et seq.

Thrombo-angiitis

Symptoms of intermittent claudication usually present.

Trophic disturbances almost always complicate, often ulcers and gangrene; always associated with pulseless vessels.

Predilection for young Hebrew males.

Slow progressive course, first gangrene of one, then often of other lower extremity, then possibly upper involved with amputation, a sequence in large percentage.

Migrating phlebitis characteristic in a fair percentage. (Histological examination of extirpated veins yields characteristic pictures.)

Most of the confusion existing in the literature in differentiation of true erythromelalgia from the symptomatic picture of rubor complicating other, particularly obstructive, arterial disease, is due to the publication in the literature of cases of erythromelalgia with arterial lesions. An analysis of these cases will show that none of them belongs to the true nervous affection "erythromelalgia."

Hamilton¹ seems to have misinterpreted the significance of occlusive changes in the peripheral arteries of a case; and incorrectly identifies the rubor or erythromelia with true erythromelalgia. Similarly others² are in error when they describe typical cases of thrombo-angiitis obliterans as being related to erythromelalgia. It is the redness in the dependent position, a striking symptom of thrombo-angiitis obliterans, and the pain that may lead the clinician to think of erythromelalgia; and the gangrenous termination, which may cause confusion with Raynaud's disease. Individual characteristic symptoms of thrombo-angiitis obliterans do not justify us in establishing a relationship between this disease and others in which somewhat similar phenomena may be found.³

The arteriosclerotic type of obliterative vascular lesion may present *rubor* and *pain* of either upper and lower extremities. The redness is usually not a vasomotor phenomenon but due to a chronic state of compensatory dilatation of the capillaries intensified in the pendent posture. It is frequently developed shortly after attacks of recent extensive arterial occlusion, that is, after thromboses; it disappears completely on elevation of the limb, being replaced by ischemia; its degree diminishes *pari passu* with such raising of the limb through an arc of 180 degrees. The *expression test* (digital compression)

Erythromelalgia

Intermittent claudication absent.

Trophic lesions rare, come late, gangrene in type simulating Raynaud's, but *vessels pulsate*.

Females and all races equally affected.

Symmetrical distribution more frequent; prognosis better, amputation almost unknown.

Thrombo-phlebitis absent.

¹ Hamilton, Jour. Nerv. and Ment. Dis., 1904, p. 217.

² Sachs, Am. Jour. Med. Sc., 136, p. 562.

³ Similar misconceptions are found in the literature concerning Raynaud's disease; *vide* Am. Jour. Med. Sc., 1908, 136, p. 565, in which a typical case of thrombo-angiitis obliterans is referred to as follows: "It is worth noticing as etiological factors in this typical instance of Raynaud's disease." A careful study of this case will afford convincing proof that thrombo-angiitis obliterans was the lesion. See also the cases of Shaw (Brit. Med. Jour., March 21, 1903, p. 662), that are described as erythromelalgia, but belong to the organic vascular type of disease.

is followed by an abnormally sluggish return of skin color and filling of the capillaries.

Some of the arteries can always be demonstrated to be occluded. Other signs of arteriosclerosis are usually present. The affection is a slowly progressive one and may lead to trophic lesions and extensive gangrene. Ischemia on elevation, a long history of intermittent claudication, with attacks of aggravation of symptoms due to thromboses, possibly previous ulcer formation with healing—all these are significant.

Erythromelalgia with asphyxia and local syncope is a rare picture difficult to estimate correctly, and differentiation from Raynaud's may be impossible.

Erythromelalgia with marked trophic lesions will have to be regarded as a purely symptomatic concomitance of manifestations, when part of the picture is acromegaly, myxedema or scleroderma. The hypertrophy of the distal parts in true erythromelalgia is of a different order from that of acromegaly, in that bony enlargement is usually absent; then, too, the former affections present none of the typical alterations of the cranium, the cerebral symptoms (hemianopsia bitemporalis) of the latter.

Neuritis and neuralgia with their distinctive features of paralyses, points of tenderness, etc., must be diagnosticated *as such*. In the absence of such pathognomonic signs, and where erythromelalgic symptoms occur in the territory of certain nerves, erythromelalgia of the first type with isolated nerve distribution should be diagnosticated.

Miscellaneous obliterative conditions of the larger arteries of a limb may present the following complex: intensive rubor in the pendent position, paresthesiæ, pain, swelling of the fingers or toes, with or without trophic lesions at their distal ends. Such may be the manifestations of arteritis of infectious origin with occluding thrombosis; of luetic arterial disease with thrombosis; and either upper or lower extremities may be involved. In these affections, however, the radial, ulnar or brachial artery fails to pulsate, or the larger arteries of the foot and leg; ischemia can be elicited on elevation; the hand or foot is colder on the affected side, and varying degrees of atrophy are noteworthy.

Therapy.—An endeavor should be made to mitigate the symptoms. This may be accomplished by placing the limb in a horizontal position, through the avoidance of motion and of exposure to excessive temperature changes. The best guide as to position will be the experience of the patient himself.

Although cold is well borne by some, and cold water is occasionally employed by the patient to alleviate the symptoms, these may be aggravated thereby in other cases. Nevertheless the winter months seem to afford relief to some patients.

Electrical therapy is of value at times; and faradic local baths may be tried. The galvanic current with the anode over the painful part may be of some value.

A large number of medicaments have been tried with very doubtful success; tonics such as arsenic, quinine¹ to improve the general health, the coal tar preparation for the pain, and sedatives for the neurotic manifestations. Suprarenal substance was suggested by Lewandowsky² and is reported by Moleen³ as having been beneficial. Organo-therapy is not infrequently of

¹ Achard and Levi report recovery in a case following the use of this drug (Semiologie Nerveuse, p. 580).

² Lewandowsky, Quoted in the United States Dispensary, Ed. 19, p. 583.

³ Moleen, Jour. Am. Med. Assn., Aug. 17, 1912, LIX.1

value, if the existence of an endocrine dyscrasia in the case under consideration can be established.

The Foerster Operation.—Resection of the posterior nerve roots is an operation suggested by Foerster for spastic paralyses, erythromelalgia and gastric crises.

In a case of erythromelalgia reported by Mayesima¹ a favorable result was obtained by this method. The author describes the operation as follows:

With the patient in the prone position, a median longitudinal incision was made from the ninth dorsal to the third lumbar vertebra, the spinous processes laid bare, the musculature displaced laterally, and the joints exposed. With the spinous processes and the laminae sufficiently removed, the posterior roots were brought into view. After splitting the dura, a longitudinal incision was made in the dura, the fourth and fifth posterior lumbar, and the first and second sacral roots exposed, and about 1 to 1½ cm. of each resected. Closure of the dura incision and suture completed the operation (no changes were found in the resected nerves histologically).

In this author's case, a young woman (24 years) suffering from erythromelalgia of the upper and lower extremities, the tips of the toes would become violaceous or red. The discoloration progressed centrally, becoming gradually more and more intensive and attended with increased local temperature. The toes, dorsum of the foot and part of the leg were involved, these areas being the source of exquisite pain.

About 5 months after the operation, the author reports complete absence of attacks of pain, heat and discoloration, but anesthesia of the right foot, and diminished sensation of the left.

Opinions of the authors regarding various modes of treatment must be critically analyzed, since cases of organic vascular disease are not infrequently mistaken for this affection.

CHAPTER XCVII

THE ACROPARESTHESIAE

This affection, first designated as acroparesthesia by Schulze,² but previously described in somewhat different form by Nothnagel, comprises the following manifestations:

1. Paresthesiæ, such as formication, feeling of numbness, and creeping sensations.
2. Pain of a tearing, variable character, not limited to the territory of a nerve.
3. Disturbances of sensation including hyper- and hypesthesiæ; and
4. Vasomotor phenomena, such as coldness and pallor of the skin.

In the variety of combinations presented not any one of the above symptoms seems to take a dominant part in the complex, although there are acroparesthesiæ without any of the other manifestations in some. Associated pain phenomena may play just as an important rôle in others.

It may be of some clinical value to differentiate the cases of pure acroparesthesiæ from those attended with vasomotor or even trophic disturbances. The objective sensory manifestations of moderate degree may be present or absent in either of these forms, and so also may pain be wanting or a prominent symptom.

¹ Mayesima, Deutsch. Ztschr. f. Chir., Heft. 1 u. 2.

² Schulze, Deutsch. Ztschr. f. Nervenhe., 1892, III, p. 300.

Haskovec¹ distinguishes 3 groups: (1) paresthesiæ without vasomotor symptoms; (2) paresthesiæ with secondary vasomotor, usually vasodilator symptoms, and sometimes trophic disorders; and (3) secondary paresthesiæ with primary vasomotor changes (as in Nothnagel's case).

Clinical Course.—An observation described by Haskovec may illustrate.

A woman 62 years of age complained that the right hand would "fall asleep" and would then become useless. Later, swelling of the wrist joint appeared with a regional herpetic eruption. The fingers were reddened and slightly edematous. Objectively there were no sensory disturbances. Formication and creeping sensations, too, were complained of. After electrical treatment, the redness and swelling disappeared, but the paresthesiæ persisted.

In the cases of Nothnagel the sensation of numbness, a dead feeling with pallor, and coldness of the fingers were the characteristic manifestations.

In 14 cases, all of which were females, there was usually a gradual development of paresthesiæ (deadness and numb feeling) as if the fingers were absent, had fallen asleep, or were the seat of tearing pain and peculiar prickling sensation. The fingers, hands and anterior aspect of the forearm felt cold in varying degrees, and the tactile sensations were somewhat disturbed. Objectively there was diminished sensation to needle pricks, as well as to temperature and electrical stimuli. The disturbances were usually bilateral, and not confined to the territory of any nerve; whilst the mobility was unimpaired, except in so far as slight stiffness impeded the action of the fingers. The fingers were pale, white, and somewhat cadaveric in appearance.

The symptoms were usually most marked in the morning and most prominent in cold weather; rubbing and hot water would bring about a certain amount of relief.

Although the affection usually begins gradually, some instances of acute onset have been reported (Friedmann²). Whilst in the latter the duration may be only one or a few weeks, in most of the reported examples a chronic, recalcitrant type is described. In such the manifestations last months or years.

The signs and subjective sensations are most marked in the morning. Some authors mention the effect of hot water in evoking the attack, and in rare instances cold. The carrying of objects, or the dependent position of the hand may incite the symptoms.

Analysis of Symptoms.—Amongst the paresthesiæ may be mentioned sensations of creeping, formication, itching, feeling of deadness as if the parts had fallen asleep; at times severe pain sufficient to awaken the patient and necessitate morphine. Such symptoms are apt to appear in attacks, either during the night or in the morning; during these the motility may be somewhat restricted. Usually both hands are involved; and more rarely the feet. The paresthesiæ, however, are not confined to the territory of any peripheral nerve.

Objective Sensations.—In most instances the sensory qualities are intact, although hyperesthesia and hyperalgesia have been reported. Cassirer mentions hypesthesia as being occasionally present.

Motor symptoms are either absent, or of very slight degree. Some of the patients complain of irritative motor symptoms, such as contraction during the attack. The reflexes are normal.

Vasomotor Symptoms.—Most of the recent authors describe cases in which paresthesiæ and pain are combined, possibly with some slight sensory disturbances, while Nothnagel's observations include instances of associated vasomotor phenomena. Local syncope does not properly belong to the complex *acroparesthesia*. Indeed, when the vasomotor symptoms become

¹ Haskovec, Wien. klin. Rundschau, 1897, 43.

² Friedmann, Deutsch. Ztschr. f. Nervenhe., 1893, p. 450.

prominent, we are dealing with a transition form between the acroparesthesiæ and Raynaud's disease.

Pathogenesis.—The paroxysmal appearance of these manifestations would lead one to conclude that the responsible agent is one that must accumulate to produce its periodic influence. In this sense it resembles the neuralgias, except that in the latter intensive pain referable to the territory of certain nerves, and the painful points over the nerves with redness and hyperhidrosis are significant signs. Perhaps we can assume that there is an abnormal weakness of the nervous system that makes it unable to resist certain deleterious factors, and, indeed, it may be assumed that the vasomotor nervous system is here also in a condition of hypersusceptibility. Up to the present time explanations of the malady are based on hypothesis alone. Cassirer suggests that the sensory nerve endings, or those of the sensory vascular nerves, are affected; or that there is a disturbance of the vasoconstrictors, in view of the occurrence of cases with pallor and coldness. According to this conception the acroparesthesia of the Schulze type (the simple form) represents a sensory neurosis; that described by Nothnagel a vasomotor sensory neurosis. In the former type the peripheral, sensory nerve endings of the skin and vessels are involved; whilst in the latter the peripheral, vasoconstrictor nerves are the seat of the disease.¹ In the latter the symptoms are brought about either directly or reflexly.

Prognosis.—The disease may last for months or years without deleterious consequences; or the symptoms are acute and may rapidly subside. The health may be considerably impaired in the chronic variety.

Therapy.—Treatment with electricity, especially Faradic current or Faradic hand baths have been recommended. Symptomatically these methods seem to be of some value. Hydrotherapeutic measures, including warm or cold local baths or douches of alternating cold and warm, have been rewarded with some success.

Of the many forms of medication tried, the tonic treatment (including arsenic, phosphorus, and strychnin) is worthy of a trial. Quinin has been suggested, and arsenic is believed to be of special value for the vasomotor symptoms.

CHAPTER XCVIII

GANGRENE WITHOUT ORGANIC VASCULAR DISEASE

There are still many clinicians who are of the opinion that gangrene of the extremities must depend upon some organic derangement of the patency of the arteries or veins, regarding those scant reports of Raynaud's disease, in which changes in the vessels have been found, as being irrefutable testimony in favor of their own view. An analysis of such references in the literature has convinced the author that no distinct causal relationship between the vascular lesions and the symptoms has been definitely established in any of the reported cases. Furthermore, in the course of studies on arterial disease amputated material was obtained from cases of gangrene in which all the vessels were pulsating. Here an opportunity was afforded to prove conclusively that even extensive, spontaneous gangrene can occur without organic vascular disease. In order to dispel all doubt as to the possibility of the

¹ Müller does not agree with the views expressed by Cassirer and would explain all the acroparesthesiæ on a vasoneurotic basis.

occurrence of *gangrene* in the absence of vascular disease, and to clarify the concept of this type, the histories of pertinent cases are here recorded.

CASE I.—*Sensory and Vasomotor Phenomena of Both Lower Extremities, Gangrene of Small Extent with Pulsating and Normal Vessels.* M. R., male, Russian Hebrew, 40 years of age, was first examined by us on November 24, 1908. As far as can be elicited, there are no nervous stigmata; habits good, very little alcohol, smoking moderate. Some 6 years ago he remembers having had some "trouble" with both feet. There were periods of weeks and months during which the toes of both feet became exceedingly painful, the big toes being first affected, followed by successive involvement of each and every toe of both feet. He is not certain that the toes were discolored, but believes that they had a tendency to become blue. There was no pain in the leg and foot on walking. These symptoms would pass off after 2 or 3 months, and did not reappear for almost 9 months. He distinctly remembers a severe recurrence after this interval, but the relapse was not of as long duration as the initial attack. He has been free from all symptoms for almost 4 years.

In August, 1906, he was first attacked with severe pain in the middle toe of the left foot. The toe became discolored, intensely blue and slightly swollen. Gangrene set in within 3 weeks and in September the toe required amputation. There had been no trouble in walking or any ache whatsoever, nor can the patient think of any cause for the affection, such as injury, exposure, etc.

In June, 1907, there was pain in the toes of the right foot, the fourth toe soon becoming blackish, an ulcer resulting after the separation of some mortified skin.

In September, 1908, the middle toe of the right foot and the little toe of the left foot developed similar manifestations with small areas of gangrene.

Examination, November 24, 1908.—Left leg: The third toe has been amputated at the first interphalangeal joint. The fifth toe is cyanotic over its distal half. Otherwise the color of the foot is normal. *All the palpable vessels of the foot and leg, the dorsalis pedis, posterior tibial, the femoral and the popliteal pulsate strongly.* Right leg: There is marked cyanosis of all the toes, particularly of the third toe even in the horizontal position. In the pendent position, the cyanosis gradually deepens, but absolutely no evidence of rubor or erythromelia can be elicited. In the horizontal position, the tips of the third, fourth and fifth toes are purple, but apparently less so than when examined some two weeks ago. There is a superficial patch of gangrene over the third toe, and the fifth toe shows the deepest blue discoloration. *All the vessels pulsate, the dorsalis pedis, posterior tibial, popliteal and femoral.* In the elevated position, it is difficult to determine whether ischemia is present or not. At any rate, it is not sufficiently marked to be diagnostic. In the pendent position, the right leg becomes more blue, the veins stand out very prominently and, at times, one can see a certain amount of rubor which is not typical of thrombo-angiitis obliterans. The same phenomena are present when the left leg is examined in this position; the pain becomes more marked, to such an extent that the patient cries for relief wishing to bring the foot back to the horizontal position. Sensation is practically normal over both feet and even the gangrenous toe has sensation, except over the mortified area. Nerve status, negative (no evidence of syringomyelia). Thus the symptom-complex is mainly characterized by cyanosis of the toes and foot, gangrene of slight extent with pulsation of all palpable vessels.

On December 29, 1908, the patient was again admitted to the hospital. He says that for more than a month the little toe of the left foot has troubled him, the bluish color persisting, till gangrene finally set in.

Physical examination shows dry gangrene of the distal half of the little toe of the left foot. Now, too, the striking signs are the pulsation of the vessels, cyanosis and gangrene.

January 4, the little toe was disarticulated and within a month the wound was healed.

In brief, a case in which, after a prodromal period of attacks of sensory disturbances in the lower extremities, there supervened paroxysms in which sensory and vasomotor disturbances made their appearance. These in their turn gave way to dry gangrene, the toes of both feet being affected almost symmetrically. The absence of the typical ischemia, of erythromelia and of any evidence of obliteration of the vessels, excludes the diagnosis of thrombo-angiitis obliterans; we may, therefore, assume that we have here, either a case of atypical Raynaud's disease or of so-called "acroasphyxia." But even belonging to the latter it would be a variant form.

CASE II.—*Paresthesiæ, Chronic Cyanosis, and Pain Terminating in Gangrene; All Palpable Vessels Pulsating.*—M. S., 50 years of age, male, Russian Hebrew, admitted to the hospital February 13, 1909; traveling salesman; in this country 4 years. Habits good, smokes ten cigarettes daily, married, four children, denies lues. He thinks that about 13 years ago, he had symptoms in the right hand similar to those that now affect his left leg. The finger tips were blue and cold, and there was a feeling of "pins and needles," with occasional pain, lasting for almost 2 months.

About 6 months ago his right leg began to trouble him, and the second toe became very blue, but the symptoms all disappeared upon internal medication. Three months ago he began to experience peculiar sensations in the toes of the left foot, and the third and fourth toes became very blue. In addition to the pain and cyanosis, there were peculiar sensations in the toes and in the ball of the foot, as if they were pricked by needles. As time went on these pains increased so that they finally became almost unbearable in the pendent position of the leg. As for the general symptoms, he complains of frequent dizziness, and attacks in which spots appear before the eyes.

Physical examination: The patient is a well nourished male; heart negative; radial pulse somewhat thickened. Left leg: The third and the fourth toes are distinctly bluish, the foot is cold; *all the palpable vessels are found to pulsate distinctly*. Right leg: There is slight cyanosis in the pendent position. Wassermann reaction negative; blood varying between 150 and 175 mm. Nerve status: no evidence of any organic nerve lesion can be detected on complete examination of nerve status.

Examination, February 24: Left foot: Cyanosis of the left foot has considerably deepened in the horizontal position; the third, fourth and fifth toes are very blue, and on the plantar aspect suggest that these are the seat of the impending gangrene. *The dorsalis pedis, posterior tibial, popliteal and femoral arteries pulsate strongly*. There is slight edema of the forepart of the foot.

March 4, 1909: Now the third toe of the left foot over its distal phalanx is distinctly gangrenous, the foot and ankle are very edematous, although all the vessels can be felt pulsating. There is no marked erythromelia, no marked ischemia in the elevated position.

March 7: The second and third toes of the left foot are now completely gangrenous; the fourth toe shows a patch of superficial gangrene over its plantar aspect; the big toe is slightly cyanotic, but shows no evidence of gangrene. The edema of the foot is increasing considerably.

In short, within a period of 4 months, the symptoms being cyanosis and pain in the left foot, there finally developed gangrene of three toes. Because edema was rapidly increasing over the foot and leg, and the gangrene bid fair to extend rapidly, and because of the intense, almost unbearable pain, it was decided to amputate, so that on March 11 the leg was ablated through the upper fourth. *The larger vessels were found patent* and required ligation. None of the usual appearances so characteristic of the vessels in thrombo-angiitis obliterans were found, and no evidences of thrombosis discovered at the point of section.

On the following day, secondary hemorrhage occurred. The patient was taken to the operating room and the vessels caught and tied.

On March 24, 1909, because of sloughing of the skin and absence of any tendency to heal, reamputation was done, after which the wound healed slowly, the patient being discharged on May 18, 1909.

Summarizing the important features of this interesting case, we may say that in a patient in whom some thirteen years previously there has been a distinct history of vasomotor phenomena in the upper extremities, and in whom, some six months ago, the right lower extremity also seemed to have been involved in a similar way, there finally developed the following symptom-complex in the left leg: paresthesiæ, pain and asphyxia or cyanosis of the left foot. After a period of four months, in which the pain became more and more severe, the cyanosis involving three of the toes deepened, finally terminating in gangrene. All of the vessels that can ordinarily be palpated were found distinctly pulsating and at operation proved to be patent at the point of ablation.

The material from the case was particularly valuable for the pathological investigations. In Case I, the author was only able to obtain the little toe for examination; in Case II, however, the foot and lower two-thirds of the leg were carefully dissected and practically all of the larger arteries, veins and nerves preserved for microscopic examination, as well as the tissue of four of the toes. A thorough study of the larger nerves in Case II with the usual histological methods, was included in the microscopic research.

In addition to the vessels of the toe in Case I the following arteries and their accompanying veins were completely dissected out in continuity in Case II, and a larger series of microscopic sections made: the posterior tibial, anterior tibial, the plantar arteries, dorsalis pedis, their venæ comites, and the

internal saphenous vein through their course, and all of the tissue save the bone of the second, third, fourth, and fifth toes.

Except for slight thickening of the walls of the veins and arteries in a few places, and an occasional sign of the earliest atherosclerotic changes, *the vessels were practically negative throughout; nowhere were they occluded.*

Only few arteries leading into some of the gangrenous areas showed recent thrombosis, doubtless as a sequence of the mortifying process. Some interesting observations were made on the minute vessels in the subcutaneous tissues. Marked proliferation of capillaries was noted in places.

The following nerves were examined: the internal and external plantar, the anterior tibial, the posterior tibial, and branches of the peroneal nerve. In none of these could degeneration be detected. The Marchi and Bielschowsky were the methods employed in searching for degeneration.

In short, there were neither lesions in the nerves nor in the arteries and veins that were in any way related, or could be held responsible for the gangrenous process in either case.

CHAPTER XCIX

RAYNAUD'S DISEASE

In spite of the extensive literature on Raynaud's disease, the practitioner still finds great difficulty in recognizing this malady, and particularly in differentiating it from thrombo-angiitis obliterans.

Raynaud in 1862 was one of the first to maintain that gangrene could occur without vascular occlusion in his monograph entitled "*De l'asphyxie locale et de la gangrène symétrique des extrémités.*"

A careful clinical study of the various forms of sensory, vasomotor and trophic neuroses would suggest the recognition of a clinical group in which sensory symptoms (paresthesiæ) predominate—as in the *acroparesthesia* of Schultze—and a group in which vasomotor and sensory phenomena are combined (Nothnagel's *acroparesthesiæ*).

Whilst in some of the vasomotor neuroses to which Raynaud's disease properly belongs—for example, in the simple *acroparesthesiæ* (Schultze) and Nothnagel's neurosis—sensory and vasomotor disturbances are the chief phenomena, and whilst in erythromelalgia, trophic disorders may be superadded, it is characteristic of Raynaud's complex that *neurotrophic* alterations are amongst the most important features of the malady.

Before entering into details we may clarify and facilitate our previous concepts by accepting the following clinical characteristics as those of a typical case. Cassirer concisely puts it as follows:

Somewhere in the peripheral portions of the body (so-called acra) there occurs more or less severe pain. This is not confined to distinct nerve territory, usually affects symmetrical parts. Attacks of vasomotor and trophic disturbances are part of the syndrome, to wit: (1) syncope, asphyxia, or local rubor, and (2) severe trophic disturbances, usually in the form of gangrene of the parts first affected with symptoms. The course is an intermittent one, for there may be completely free intervals; but in some instances, evidences of disturbed vasomotility may persist. The disease may consume itself in one attack or several

attacks may occur in succession. Objectively, sensory disturbances are usually absent, as well as paralysis, although other evidences of disturbed vasomotor innervation, aphasia, hemoglobinuria, and arthropathies, may occur. Usually neuropathic individuals are affected.

Clinical Picture.—There is usually a story of psychic insult or exposure to cold in young women, and then the advent of the stage of *local syncope*, in which certain symmetrically situated peripheral portions of the body become ischemic and blanched. This gives way to a period in which peripheral cyanosis is characteristic (*local asphyxia*). Or, a combination of both occurs, so that patches of whiteness and of lividity are contiguous. Accompanying these phenomena are paroxysms of pain, or, at times, anesthesia of the corresponding parts. Tingling, burning, formication and other paresthesiæ, with the substitution of lighter areas for the cyanotic patches, usually signalize the abatement and subsidence of an attack.

Such cycles of symptoms recur at varying intervals until the symptoms in the milder cases completely disappear. In other patients, however, typical symmetrical gangrene develops. As the cyanosis deepens, the skin at the so-called acra (tips of fingers, toes, ears) becomes deep blue or almost black. Then dry necrotic areas of skin develop which scale off, the underlying parts receding so as to leave retracted scars. Although this is the typical clinical course and symptomatology, a great number of variations are encountered, in which either the syncope or the trophic disorders play an insignificant rôle.

An interesting example of Raynaud's, in which the diagnosis can be made although the clinical phenomena do not adhere in all particulars to the type, is the following case in which both upper and lower extremities were implicated.

E. M., 54 years of age, female, believes she has had attacks for many years, possibly ten. Her feet and hands would get suddenly cold and white, the fingers and toes would become painful and then deep blue followed by red.

Observation by the author on February 1, February 2, and February 15, 1911, may be worthy of perusal.

February 1, 1911: The patient is in an attack, but believes it to be subsiding. Both hands are cold, the tips of the fingers red. The dorsal aspects of the second phalanges are very white. The color changes rapidly while the patient is being observed, the blanched portions becoming suddenly red. The fingers on palpation give a peculiar tense sensation as if moulded out of wax. The nails are deformed, and the second, third and fifth fingers of the right, and the third, fourth and fifth fingers of the left hand, at the tips, show scarring. The tip of the fifth finger (right) presents a large recent scar that is still tender.

Both radials pulsate strongly.

The vessels of the lower extremities are evidently patent. Almost all of the toes have patches of hemorrhagic discoloration that do not disappear on pressure, but at this time the feet seem to be free from an attack.

February 2, 1911: The tips of the fingers are cadaveric; both radials pulsate well.

February 15, 1911: The fingers of both hands show a mixture of cyanosis and extreme pallor and are very cold. As they are watched for a few minutes, a bluish discoloration of the third, fourth and fifth fingers comes on, and varies with alternating areas of rubor and pallor.

The fingers of the right hand remain waxy and cadaveric. The nails appear white, the distal portions of the phalanges cyanotic. The dorsal surfaces of the second phalanges are blanched, the knuckles are cyanotic. Both radials pulsate during this period. A few minutes later the index finger of the left hand up to the first interphalangeal articulation becomes cyanotic and remains so, although color has returned into all of the other fingers. While the fingers were cyanotic, sensation was much diminished (almost absent) and returned on the advent of normal color.

The tips of the toes were found livid. During a short period of observation there was a play of color over the feet, an interchange of cyanosis and rubor.

A case approaching more closely to the classical description, although somewhat atypical, is the following:

Raynaud's Syndrome in Young Woman, with Upper Extremities Involved.

R. S., age 38 (referred Jan. 4, 1917), married nine years, three premature labors, one child born seven and a half years ago is well.

Fourteen years ago she is said to have had severe dysmenorrhea, the ailment of which she now complains, and which involved her hands, appearing about that time. She believes that blueness and coldness of the finger tips particularly on exposure to low temperatures were the first noticeable changes.

Then the attacks became more frequent, almost daily, with alternating blueness and pallor of the fingers of both hands, but unattended with *pain* until two years ago, when this symptom became an integral part of the malady. During each of three pregnancies, a remarkable improvement was noted, the attacks returning immediately after confinement.

Simultaneously with the discoloration, a puffy condition of the fingers comes on and some changes have occurred in the skin at the tips. She has noted that whenever the symptoms in the extremities are most marked, gastric disturbances occur: such as vomiting of almost all ingested food; these would cease immediately upon the cessation of the attacks in the hands.

Physical examination: All the fingers of the right hand are somewhat swollen, except perhaps the little finger. There is very slight puffiness of the fingers of the left hand. There are evidences of trophic disorder at the tips of the index and middle fingers of the right hand in the presence of small, dry, brownish scabs. The index finger of the right hand has a brawny feel, induration being distinct, and less marked over the tip of the middle finger, and still less over the tip of the ring finger.

As the hands are watched, variations in color take place. At times the middle and index fingers of the right hand particularly become markedly cyanotic, the corresponding fingers of the left hand similarly affected but less so. A play of color takes place from time to time, cyanosis giving way to redness, which involves the greater part of the fingers affected. These changes take place so rapidly that a cycle of variations from blue to red and red to blue consumes a period of two or three minutes, or less. Spots of blanching appear from time to time.

Pulses.—Radial and ulnar pulses are distinct. X-ray examination of the hands reveals a disappearance of the distal portion of the terminal phalanx of the index finger of the right hand; and a suggestion of incipient and similar changes in the left index finger.

Lower Extremities.—In the horizontal position there is slight cyanosis of all the toes of the left foot, most marked in the big toe, associated with some blanching of the proximal phalanges; the sole is cyanotic. Right foot is normal in color.

Dorsalis pedis and posterior tibial arteries of both feet pulsate.

Although many attempts have been made to cast doubt on the existence of the morbid entity of Raynaud's disease, the author agrees with those who believe that an independent, intrinsic or idiopathic affection can be and should be recognized under that name. It is true that some of the manifestations occasionally coexist as symptoms of other affections usually with central or peripheral nerve disease, but this is of relatively rare occurrence. This association has been noted especially with spinal cord tumors, syringomyelia and neuritis, also with a number of instances of psychoneurosis. When such is the case, we are dealing with a mere symptomatic coincidence that does not warrant the diagnosis of the true disease.

Nomenclature.—Because the pathogenesis is so little understood, attempts to apply descriptive names have been unsatisfactory. Certain authors take issue with Raynaud's descriptive title—"Asphyxie locale et gangrène symétrique des extrémités"—on the ground that both asphyxia and gangrene may be absent. "Angiospastic gangrene" is criticized as implying the acceptance of a mechanism to which all authors do not subscribe. Thus, it may be best to adhere to the name "Raynaud's Disease," reserving such designations as "Raynaud's Phenomena" and "Raynaud's Symptoms" as denoting abridged, variant and incomplete pictures of the disease.

Incidence. *Age.*—According to Raynaud, most of the cases occur between ages of eighteen to thirty years. Morgan¹ found an average of

¹ Morgan, The Lancet, 1889, II, p. 9 ff.

26.6 years in his ninety-three cases; Monro put this at 28.9 years. Of the hundred and sixty-eight cases collected by Cassirer there were fifty-five in the first and second decades as against forty from the age of twenty one to thirty years. In a subsequent study of a series of one hundred and nine cases Cassirer noted that the largest number of cases were from twenty-one to forty years of age.

Sex.—Raynaud concluded that four-fifths of his patients were women; Monro found 62.6 per cent women, 37.4 per cent males; Cassirer obtained almost identical figures reporting 62.9 per cent females, 37.1 per cent males in 180 cases.

Statistics as to the relative frequency of the affection yield according to Monro 1 case to 3000 other affections. Of 7000 patients in the Neurological Clinic of Oppenheim, Cassirer found only 5 typical cases. It is more frequent than erythromelalgia, but more rare than the other vasomotor and trophic neuroses.

Cold seems to influence the development of the disease and it has been observed to be of frequent occurrence amongst washwomen.

Etiology.—A neurotic constitutional disposition of hereditary nature predisposes to this affection. Anemia sometimes seems to play a rôle, whilst in other cases, the general nutritional condition is excellent. Sexual and menstrual disturbances do not appear to be without influence according to Raynaud.

Trauma has been held responsible (Cramer¹), so also psychic exertion, sudden fright, cold, wet, acute infections, and a neuropathic constitution.

It will occasion little surprise that in a malady of such obscure pathogenesis, the internal secretions should have been held in some way responsible. So we have a reference in the literature by Möbius² in the year 1896 to the possibility of the participation of the thyroid gland in the production of the syndrome. Solis-Cohen, too, has contributed observations and inferences bearing on the derangement of the internal secretions in the vasomotor affections. Leopold-Lévi et de Rothschild³ (1909) speak of para function (dyscrasia) of the thyroid. Voivenel et Fontaine⁴ suggested the theory of hypothyroidism consequent upon ovarian insufficiency.

Osborne⁵ holds that Raynaud's disease is not a distinct entity, but a syndrome caused by disturbances of one or more internal secretions; that it is not dependent on primary disease of the vessels, but that the vasomotor control is deranged in such a manner that most pronounced contraction of certain blood vessels may occur in different parts of the body; that such angiospasm may occur in internal organs as well as peripherally; that there is usually a disturbance of thyroid function; and hence the assumption is warranted and confirmed in his clinical observations that the administration of thyroid gland is followed by improvement in the majority of cases.

The hypothesis that an increase of vasoconstrictor substances in the blood serum may account for arterial spasm and gangrene in "so-called spontaneous gangrene" has found certain adherents (Oppel and Girgolaf⁶); and a similar explanation has been invoked by some authors for the spasm in Raynaud's disease. Hyperadrenalism or overactivity of the adrenals is believed to be responsible for the endocrine disturbance.

¹ Cramer, Arch. f. Orth., 1909, VII, p. 431.

² Möbius, Vasomotorisch-trophische Neurosen, Penzoldt-Stintzing's Handb. V Bd., I, Aufl., p. 472.

³ Leopold-Lévi et de Rothschild, Revue neurol., 1909, p. 209.

⁴ Voivenel et Fontaine, L'encephale, 1910, II, p. 166.

⁵ Osborne, Am. Jour. Med. Sc., Aug., 1915, p. 158 et seq.

⁶ Chirurgitcheski Viestnik, 1922, No. 1, and Lancet, July 15, 1922, p. 1116.

Interesting as these hypotheses may be, incontrovertible evidence is still lacking to warrant unqualified acceptance of the endocrine nature of the disease.

The influence of thyroid therapy on Raynaud's disease has been emphasized by some authors as of etiologic import. Lévi and de Rothschild¹ have called attention to the association of Basedow symptoms in this affection, and *per contra* the total absence of myxedema in any of the reported cases. Thus, they believe a thyroid dyscrasia is a factor in the production of the disease.

Symptomatology.—We may divide the clinical course into three stages: firstly that of *vasomotor symptoms*; secondly, that of marked *trophic disorders*, and thirdly; the period in which *gangrenous sloughs* or *necroses* are detached, local healing usually taking place with the subsidence of symptoms.

The Stage of Vasomotor Phenomena.—Here belong the characteristic local syncope and asphyxia.

Local syncope, when it affects a peripheral part, is characterized by sudden blanching and coldness, of varying intensity from cadaveric white to combinations of color, shadings with greenish bluish and red. A reduction in temperature of the part, and sensory symptoms are associated. Pares-thesiæ and pain that follow or sometimes precede the syncope are variously described. Numbness, formication, radiating aches often give way to intense pain, accompanied by the sensation of a local benumbed or dormant state. In other cases only paresthesiæ are noted. More or less rigidity or clumsiness of the fingers, when these are affected, associated with cold perspiration complete the picture of this stage.

The pallor has been described as waxy, tallowy and dull, being rarely absolutely white, though a yellowish tint is not uncommon. More frequently than this discoloration does the numbness and blunting of the sense of touch strike the patient's attention; for it interferes with delicate movements.

Strange to say, while occasionally encountered at the extremes of life, local syncope is chiefly seen in the period of active sexual life. In a case of the author, as also in one recorded by Raynaud, the liability to local syncope always ceased during the early months of each pregnancy.

Emotions, worry, exposure and fatigue seem to incite a fresh attack; other motivating agents being water, especially if cold, or even the handling of cold articles. In some cases it may occur at any hour without obvious reason. Monroe speaks of the association of flushing of the face with pallor of the fingers. This may occasion great mental distress to the patient, especially when such changes occur at meal times and are conspicuous to others.

Monroe's² tabulation of clinical data in 176 cases; records 3 in which local syncope was alone observed; 20 in which it was associated but not always synchronously with local cyanosis; and 66 other cases in which necrotic and sclerotic processes were added to the local syncope—almost always, but not invariably after a stage of local cyanosis. On the other hand, there were 28 cases in which local cyanosis alone was observed, and 56 other cases in which neurotic or sclerotic changes followed upon local cyanosis without any stage of local syncope being noted.

The Local Asphyxia.—The color of the skin changes to a bluish, purplish, violaceous hue, or may have a blue-black tint admixed with red. The adjacent parts have marmorated appearance. Here, too, a fall of local temperature is to be expected.

¹ Lévi et de Rothschild, *La petite insuffisance thyroïdienne*, Paris, 1913.

² Monroe, T. K., *Raynaud's Disease*, Glasgow, 1899.

The usual distribution is over either the fingers, toes, tips of the nose, or ears. Pressure upon the affected part with the examining finger demonstrates how sluggish is the return of blood.

A certain degree of swelling is rarely missed during this phase, whilst with the syncope, a slight contraction of volume is usual. The enlargement or puffiness is not due to edema, and may appear simultaneously with or precede the asphyxia. When it is extreme, which is rare, it should be regarded as of angioneurotic nature.

The degree of fall of temperature may vary in the fingers. Most interesting is the observation of Hoesslin,¹ who found on actual measurements that the temperature of the asphyctic part may drop some 4° C. to below that of the air.

A diversity of tinting has been reported ranging from typical asphyctic and livid hue to a fuchsin or crimson discoloration of areas that are sharply demarcated from their surroundings. Intense rubor may follow in the wake of the asphyxia, last for hours, thus mimicking erythromalgia. This color, however, is never that of hyperemia, but rather of a rose or bright red.

The syncope and asphyxia may occur simultaneously; certain phalanges may have a gray-blue or ashen gray and blue tint, adjoining other phalanges in which blanching can be observed. A play of colors with many shadings from cadaveric white into several tints of red, and the different asphyctic changes mentioned above, is not an uncommon phenomenon.

As to the onset of asphyxia, the author's observations lead him to believe that it may precede the syncope or the latter may be wholly absent. Cassirer, Weiss and others report asphyxia as signalizing the onset in many cases and mention that it may occasionally completely fail to appear.

When both local syncope and asphyxia occur, the former is usually the earlier phenomenon; but in exceptional cases, where the reverse order obtains, cyanosis may yield to blanching with a disappearance of the latter after a few minutes and a return of the blueness.

The asphyctic stage may last a few minutes, hours or days, may recur once or more often during the day or after intervals of days. On the whole, its duration is somewhat longer than that of syncope.

As for situation, the acroterial localization is not as characteristic a feature of local asphyxia as of the syncope. It may be more conspicuous over the hands than over the fingers, or the latter may be free whilst more proximal parts are notably invaded. It may not be confined to the phalanges but may affect the hands and feet, or even the forearms and legs. Both cyanosis and syncope may occur coincidentally. For example, the distal portion of the fingers may be blanched whilst the remaining sections of the hands are livid.

Trophic Disorders and Gangrene.—Usually a small bleb with sero-sanguineous or blackish content develops at the tip of one of the fingers. When this opens, small erosion or ulcer remains for a variable length of time, till it cicatrizes. Or there is dry dystrophic process in which a dark scab forms and subsequently becomes detached in a scale-like manner. Another type of trophic change begins as a sort of induration and thickening at the finger tip, with consequent detachment of scaly epidermal masses; or larger blebs may burst, giving way to blackish necrosis of the skin on the separation of which deeper ulcers are disclosed. Although a dry gangrenous process is the rule, wet gangrene may occasionally develop.

¹ Hoesslin, München. med. Wchnschr., 1910, p.29.

We expect to find symmetrically situated peripheral parts involved (fingers, toes, ears, nose) over limited areas. Occasionally, however, such symmetry is missed, and the affection has been known to implicate the sternal and buccal regions. In very rare instances large portions of a limb have become gangrenous.

Monro's¹ statistics regarding the relative frequency of gangrene in various situations are: In 43 per cent the upper; in 24 per cent only the lower; and in 22 per cent both upper and lower extremities.



FIG. 167.—Disappearance of the terminal phalanges in an case of a sclerodactyly and Raynaud's disease.

The Osseous Changes.—Characteristic changes are demonstrable in certain of the bones by X-ray examination. In the hand, the marked bony atrophy with the disappearance of one, more, or all of the tips of the first phalanges are the notable alterations of diagnostic value. Trophic bony changes involving not only the tips of the end phalanges, but reported as extending as an atrophic process as far as the metacarpus, with the possi-

¹ Monro, T. K., *Loc. cit.*

bility of restitution after recovery, are almost pathognomonic lesions (Figs. 167 and 168).

Sensory symptoms according to Raynaud are striking features of the symptom-complex, attaining considerable intensity during the stage of asphyxia, and abating with the period of reaction when paresthesiæ appear. Some writers minimize the rôle of pain, whilst Cassirer and the author are inclined to subscribe to Raynaud's views.



FIG. 168.—Changes in the terminal phalanges in Raynaud's disease.

The pain may initiate the attack or may come on during the asphyctic stage; it may begin with severity or attain the maximum gradually, the degree being occasionally so great as to warrant injections of morphine. The pain has this in common with that of erythromelalgia and the acroparesthesia, that it is not confined to the distribution of single nerves, but is diffused over the affected extremity in regions roughly corresponding in extent to that of the vasomotor and trophic disturbances. In many cases investigated in this regard, no accurate localization of the sensory, irritative and the deficiency symptom could be determined. The pain was always of a different

type than that of neuritis. Indeed, the belief has been expressed that the character of the pain and its close relationship to the vasomotor phenomena warrant the conclusion that *vasosensory fibers* may be involved; and that these may be irritated either in the periphery or from some central point.

Regarding the objective sensory disturbances these, too, are not limited to any particular nerve. In many cases they are absent. When present, hypesthesia or anesthesia are the most common, although most remarkable varieties and combinations have been reported: thus anesthesia of parts affected by syncope, with no sensory alterations in the free intervals; tactile changes and hypesthesia of all varieties over the whole hand, hypalgesia and thermohypesthesia.

As for the motor disturbances, paralyses are not observed except in exceptional instances where muscular atrophy follows, and in which the interossei and muscles of the thumb participate.

Remote Clinical Phenomena.—Occasionally there are interesting manifestations of manifold types in territories quite remote from the peripheral parts heretofore described as implicated. It has been recently observed¹ that fall in blood pressure, diminution in the number of leucocytes, and acceleration of the blood clotting time occur during the attacks in Raynaud's disease. The left cervical sympathetic nerve was affected in a case of Weiss, the left cheek becoming suddenly warm and red, associated with retraction of the left eyeball, hyperhidrosis and contraction of the pupil. A recession of all manifestations except for slight retraction of the eyeball was complete within a week, but recurrences took place, until finally a sort of partial atrophy of the soft parts of the left side of the face remained.

Arthropathies with effusions into the joints of the fingers and knees; transitory disturbances of speech; cardiac palpitation, contraction of the retinal arteries are mentioned amongst the remote symptoms.

Arterial Pulsation.—The radial artery is said by some authors to become pulseless during the stage of syncope, and this circumstance has been attributed to the arterial spasm. As a rule, however, the arterial beats can be elicited even though a diminution of force and some acceleration occur. Westphal has described, and erroneously grouped under the designation "Intermittent Claudication," a case in which the pedal pulses disappeared during an attack.

Other Evidences of Vasomotor Instability.—Amongst the many signs of vasomotor lability and neuroses associated with Raynaud's disease are the following: A neurotic temperament with tendencies to emotional outbursts; attacks of migraine and polyuria with or without symptoms of hyperthyroidism; transitory or fugitive edema and urticaria; a marmorated skin; the associated complex "epidermolysis bullosa hereditaria" (Linser²) with its tendencies to bulla formation and gangrene of the skin upon exposure to cold; multiple small epidermal hemorrhages; hemoptysis and hematemesis; chorea; and epileptiform attacks.

Demonstrable Phenomena.—Although the production of pallor on elevating the limb to the vertical is usually a distinctive feature of the obstructive diseases of the arteries, it can be occasionally evoked in the spastic vasomotor affections. In a case of Raynaud's disease of the upper extremities³ ischemia and even reactionary erythromelia were elicited during the paroxysms on several occasions. We cannot, therefore, except with certain reservations,

¹ Souques and Moreau, Bull. de l'Acad. de Méd., 84, 1920, p. 44.

² Linser, Arch. f. Dermat. u. Syph., 1907, LXXXIV, p. 6.

³ See p. 544, case R. S.

accept these artificially produced phenomena as absolutely pathognomonic for the obstructive types of arterial disease. There is this distinguishing feature, however, that these responses are demonstrable only *during the paroxysm* in the vasomotor neuroses, and whilst they can be constantly evoked in the obstructive arterial affections, and even in the former, they occur only when a spastic condition in the larger veins does not impede the return. And so, when confronted with the early vasomotor stage of thrombo-angiitis obliterans with pulsation still present, and involvement of but restricted arterial territory, the development of a continuous phase of response to the gravity tests is pathognomonic; occasional ischemia on elevation during attacks of vasomotor spasm may lead to erroneous conclusions. In the Raynaud complex, then, the hyperexcitability for vasoconstrictor responses may be motivated, perhaps, by this minimal gravity depletion.

Another interesting difference between the angiospastic and obstructive arterial affections is the circumstance that reactionary rubor or hyperemia can be produced in the neurotic types even in the vertically elevated position of the limb (after release of tourniquet). From this the conclusion can be drawn that whilst diffuse vasoconstriction may be present sufficient to manifest itself as slight ischemia on elevation, the hydrostatic factors can be overcome. Evidently the degree of functional impediment to the flow of blood is not too great in the larger channels. The arterioles and capillaries, too, are not in such a state of insurmountable tonic vasoconstriction that they are unable to respond after release of the tourniquet. When the same mechanical forces are brought into play in thrombo-angiitis obliterans, obstructive arteriosclerosis and other obliterative organic vascular lesions reactionary rubor is absent in the limb held up to the vertical.

These and other noteworthy phenomena are well illustrated in the notes from the following case:

On physical examination of R. S. (previously cited) both hands are found to be cold (examined under artificial light). The tips of the first, second, third and fourth fingers of the right hand are slightly cyanotic; the tip of the fifth finger red. Over the dorsal aspect of the second phalanges of the second, third and fourth fingers there looms up a patch of blanching which rapidly disappears, giving way to a slightly scarlet hue. A similar play of colors occurs over the left hand where the swelling is less marked than on the right. The palms are fairly red, except for cyanosis of the tips of the fingers. The radials apparently are less tense than they were at the last examination. The heart is negative.

On elevation of the hands, the cyanosis of both seems to diminish, practically disappearing in the right hand, yielding more slowly in the left. The patient says that elevation also improves the subjective state, inasmuch as the uncomfortable sensations of the fingers diminish; these seem less swollen, less rigid.

On hanging down, after preliminary elevation, the whole hand is red except for slight mottling due to cyanotic patches near the tips. On applying a tourniquet after elevation of the right arm, the hand becomes distinctly cyanotic, except for the fingers, which exhibit only patches of lividity. On releasing the tourniquet in the elevated position, rapid and intense reactionary erythromelia is elicited; it *involves the whole region distal to the site of constriction*. The tips of the fingers are cyanotic, the deep flush disappearing within a minute, normal color returning in about 2 minutes.

Scleroderma, Sclerodactyly and Raynaud's Disease.—Raynaud phenomena not infrequently occur coincidentally with, preceding or following the development of the indurative and atrophic stages of scleroderma and sclerodactyly. Indeed, because vasomotor disturbances are such early and common manifestations of scleroderma, a differentiation from the Raynaud complex has often been regarded as almost impossible.

Local cyanosis or local numbness may antedate by years the characteristic symptoms. Particularly in sclerodactyly are vasomotor phenomena apt to occur as prodromal signs. These are the cases in which the clinical

picture is that of Raynaud's syndrome for a long time and in which mixed types then develop, the differential segregation of the two diseases being not feasible. Local asphyxia and local syncope have been known to dominate the clinical picture for a long period in advance of the sclerodermic condition.

Since, in the course of Raynaud's disease, besides the typical trophic changes of gangrene, certain chronic dystrophic processes may be associated such as lead to induration and thickening of the skin and subcutaneous tissue, it is little wonder that the similarity of the two affections can be very close. For the recognition of such intermediary types, Cassirer suggests the following grouping.

1. Typical Raynaud's Disease.—This includes cases in which in addition to the symmetrical gangrene, dystrophic alterations involve the distal parts with thickening of the skin and immobilization of the tendon sheaths and joints. The skin although smooth, tense, unyielding is not typical of scleroderma; and furthermore its involvement is limited to those parts in which the vasomotor and trophic symptoms of Raynaud's are most intensely represented.

2. In this group we may gather the cases in which local asphyxia and syncope initiate the disease, with a long period of paroxysms. Instead of a further progression into the stage of gangrene, there is a chronic stage attended with abatement of the vasomotor and sensory manifestations and with the development of true sclerodermic phenomena—not only over the acra, but even implicating the face, breast, arms and other parts.

3. A third type is constituted by those relatively rare instances in which the vasomotor symptoms emerge in the midst of the completely elaborated picture of scleroderma.

To these we may add cases described by the author,¹ in which a period of vasomotor phenomena precedes the objective signs of thrombo-angiitis obliterans, both the upper and lower extremities being the sites of attack. In a second period the symptoms of thrombo-angiitis obliterans with gangrene are so well developed as to be easily recognizable, although in the case of the hands, alterations simulating sclerodactyly may finally come into evidence. Such patients suffer from true organic obliteration of the arteries, and simulate not only Raynaud's disease but also sclerodactyly in part of their clinical course.

The following differential schema has been suggested by Castellino and Cardi.²

Sclerodactyly	Raynaud's Disease
Symmetrical affection of the hands.	Symmetrical affection of the hands.
Progressive course.	Interrupted, intermittent course.
Color usually first red, less bluish.	First whiteness, then blueness.
Skin cold, hard, swollen and congested.	Skin cold, congested, swollen, not very hard.
No sensory disturbances; feeling intact.	Anesthesia.
No pain or paresthesiæ.	Severe pain and paresthesiæ.
Frequent occurrence of "sclerodermic mask."	No sclerodermic mask; if present, coexistence of two maladies.
More frequently in children.	More often in adults.

Pathology.—A study of the literature by Dehio³ and Cassirer has convinced both authors that a comprehensive adequate and satisfactory investigation into the pathological anatomy of a typical case of Raynaud's

¹ Buerger, *Am. Jour. of Med. Sc.*, Feb., 1915, No. 2, CXLIX, p. 210.

² Castellino and Cardi, *Morgagni*, 1895, I, p. 625.

³ Dehio, *Deutsch. Ztschr. f. Nervenhe.*, 1893, IV, p. 1.

disease is nowhere to be found. Where negative findings are recorded, the examinations were so incomplete as to be unacceptable. The reported arterial alterations, on the other hand, could under no circumstances be held responsible for the disease. In the various descriptions of nerve changes there are so many inconsistencies, their occurrence so inconstant that here, too, we must be chary in accepting any causal relationship.

It must be conceded that all the vasomotor neuroses, of which the Raynaud complex is a prominent example, have one feature in common, that the arteries and veins have suffered no organic alteration in their patency. The varying objective phenomena arising from vascular instability must be attributed, therefore, to some vice of innervation. We are justified in assuming that an irritative (possibly paralytic) process in the vasomotor system is responsible. According to Cassirer, "Certain parts of the nervous system (vasomotor and trophic centers and paths), particularly the vasoconstrictors, are in a condition of increased irritability, a status brought about by an abnormal congenital Anlage¹ (predisposition) whose existence is indicated by the presence of other signs of hereditary neurosis; or, a condition that may be acquired through repeated noxious influences, as frequent exposure to cold, rheumatic disease or bodily or psychic traumata; or, the irritability may be evoked through infections and intoxications or reflexly through disease of distant organs, vessels or nerves. So that although, in this way, a number of variations from the disease type are developed, the unity of the Raynaud complex is thereby not invalidated."

Diagnosis.—If the typical picture of the Raynaud complex be borne in mind, and the dignity of the phenomena be not underrated, the differential diagnosis should not be difficult. It is the atypical forms, only, which may present trying problems.

Thus, the mere presence of the so-called *doigt-mort*, or attacks of blanched cadaveric fingers, does not warrant diagnosing Raynaud's disease. On the other hand, the absence of single symptoms, even of gangrene, must not militate against such diagnosis.

A. Differentiation from Other Vasomotor and Trophic Neuroses. 1. *Erythromelalgia.*—Although some cases seem to have symptoms bordering on those of Raynaud's, a clinical distinction may be made. In both, localization, symmetry and sudden onset may coincide. However, the rubor, disappearing on elevation, the attacks of pain, the normal or increased sensibility, the very slight trophic disorders, if any, the increased temperature of the part with a feeling of warmth, the normal reflexes, *all* these should speak for erythromelalgia.

In Raynaud's syndrome, the dark bluish, purplish or blackish discoloration (in second stage) uninfluenced² by elevation, areas of analgesia, diminished sensibility or anesthesia, the well marked trophic disturbances, the diminished temperature and feeling of cold, the diminished reflexes (occasionally absent), and the rare motor phenomena (of parietic nature) are characteristic. However, that cases of Raynaud's may occasionally present certain of the symptoms of erythromelalgia cannot be denied.

2. *The acroparaesthesiae of Schultze*³ or Nothnagel form a clinical complex distinguished by the gradual or sudden onset of paresthesiae, a sensation of numbness or "dead feeling" as if the fingers were absent, occasionally formication with tearing or dragging pains, and always attended with a sensation

¹ Not in the anatomical sense.

² Note that this may not obtain in certain atypical cases.

³ Schultze, *Deutsch. Ztschr. f. Nervenhe.*, 1892, III, p. 300.

of coldness. The fingers, hands, and arms are involved. The fingers become white, colder than normal, and the radial pulses are equal and always active even though the hands are unequally affected. Disturbances of tactile sense and a diminished sensibility for needle pricks, touch, temperature and electrical irritants exist. There is a symmetrical distribution which cannot be relegated to the territory of any particular nerve. Motor disturbances are absent.

Schultze described a form without vasomotor symptoms (Schultze's type), whilst Nothnagel one with sensory and vasomotor phenomena (Nothnagel's type).

The differentiation of the acroparesthesiæ with *syncope* from Raynaud's may be difficult or impossible at times. Should cyanosis be superadded, even if only fugitive and occasional, the diagnosis of Raynaud's disease would be permissible.

3. *Acroasphyxia chronica*¹ manifests itself particularly as a gradually developing cyanosis of the end of the extremities, *without paroxysms or attacks*, associated with sensory or trophic disorders. In a second group marked trophic disorders appear, in that the soft parts are the seat of a chronic hypertrophy leading to pictures suggesting acromegaly.

Although distinguished from Raynaud's in its slow chronic progressive course, in the absence of attacks, and the permanent increase in volume of the affected parts, there are cases which seem to offer clinical transitions to Raynaud's complex. Even in these, however, pain is insignificant, and syncope absent. The temperature is diminished, the cyanosis of the hand may extend to the middle of the forearm, although the palm is less affected. The enlargement does not involve the bones.

4. *Simple Vasomotor Circulatory Neuroses*.—The incidence of a large variety of clinical symptom-complexes, particularly in women, that mimic Raynaud's disease, oft regarded as transitional stages in the development of the typical Raynaud complex, warrants a consideration and study of these conditions, so that the clinician may differentiate between maladies with or without gangrenous sequelae. From the standpoint of forecasting the future integrity of the limb in question, such diagnostic studies are of no mean importance, since the mild vasomotor neuroses are rarely associated with extensive trophic lesions.

Their differentiation from the transitory circulatory disturbances occasionally accompanying organic occlusive lesions of the vessels is readily accomplished by noting *the absence of the following signs in the vasomotor circulatory neuroses*: (1) Closed and pulseless vessels; (2) marked ischemia on elevation; (3) reactionary rubor; (4) erythromelia; and (5) chronic atrophic and dystrophic changes in the foot. Where the cases pass over into the Raynaud stage, the picture will change and the trophic and gangrenous phenomena can be expected.

B. Differentiation from Organic Nerve Disease.—1. *Atypical* nerve affections in which the diagnosis is doubtful are occasionally accompanied by Raynaud phenomena. Signs referable to organic nerve alterations should always tend to invalidate the diagnosis of a possible true Raynaud complex.

2. *Polyneuritis*, as seen in beri-beri with irritative and paralytic manifestations, may be exceedingly suggestive. Thus, loss of tactile sense, hyper-

¹ Crocq, *Semaine méd.*, 1896, XVI, p. 298.

Kollants, *Deutsch. Arch. f. klin. Med.*, LXXXVI, S. 504.

Pehu, *Nouvelle I Congr. d. I. Salpetr.*, 1903, p. 1.

Barker and Sladen, *Jour. Nerv. and Ment. Dis.*, 1907, p. 745.

Cassirer, *Die Vasomot. troph. Neurosen*, Berlin, 1912, pp. 506-535.

esthesia, absent knee reflexes with gangrene of the tips of the toes have been recorded in a case of beri-beri. Such an association of symptoms can in no wise be regarded as belonging to the Raynaud group.

3. *Syringomyelia*.—It is the trophic disturbances in this affection that may lead to fallacies of interpretation. The slow development, the absence of symmetry, the pain and characteristic vasomotor symptoms should be the distinguishing marks of syringomyelia. Summarizing the different points, Castellino and Cardi¹ attribute to syringomyelia the following characteristics: An insidious onset, a slow course over many years (10 to 15), nutritional disturbances usually involving but one limb at the onset, recurring painless paronychia, sensory disassociation, muscular atrophy, ulcer formation (perforating ulcer), loss of nails, ungual dystrophies, and necroses with sequestration of bone. Against these we find, in Raynaud's complex, a sudden onset, rapid course, symmetrical appearance, dry gangrene, anesthesia, very little muscular atrophy, and bone atrophy.

C. *Differentiation from Vascular Disease*.—The significant pathognomonic and distinctive feature of organic arterial disease is the obliteration of the usually palpable peripheral arteries. Gangrene due to cardiac and arterial disease (embolic and thrombotic gangrene), athero- or arteriosclerotic processes, and thrombo-angiitis obliterans (Buerger²) should be recognized without difficulty.³

1. *Thrombo-angiitis Obliterans*.—When this affects the upper extremities it may be readily confused with Raynaud's disease; for attendant true vasomotor phenomena independent of the classical hydrostatic and mechanical signs, may be striking features.

The symptoms simulating Raynaud's disease and acroasphyxia are cyanosis of the finger tips, coldness of the fingers with or without trophic disturbance, and alternating cyanosis and rubor, involving the fingers or the whole hand. Rather characteristic in the symptomatology of thrombo-angiitis is the apparent dependency of the vasomotor symptoms upon variations in temperature, the chronicity of the manifestations, the absence of pain in some of the cases, and the absence of paroxysmal nature of the attacks so characteristic of Raynaud's disease.

Those patients in whom the trophic disturbances seem to be unassociated with evidence of vasoconstriction and vasodilatation give merely a history of the development of a spontaneous ulcer of the fingers. It seems more than likely that in many of these the history of the absence of the vasomotor phenomena would be found unreliable if it were possible to observe the cases throughout the whole course of the disease.

Characteristic for thrombo-angiitis obliterans are the following groups of symptoms: (1) The disappearance of the pulses, particularly the dorsalis pedis, posterior tibial, and popliteal, more rarely the femoral, radial, and ulnar; (2) the development of typical manifestations of impaired circulation, to wit: blanching of the lower extremities when these are elevated above the horizontal, hyperemia (rubor) or reddening of the foot in the pendent position (a chronic condition which the author has termed *erythromelia*) during certain stages of the disease, and trophic disturbances, such as impaired growth of the toe nails, slightly atrophic condition of the skin, ulcers, and gangrene; (3)

¹ Castellino and Cardi, Morgagni, 1895, I, p. 625.

² Buerger, Jour. Med. Sc., Oct., 1908; Jour. Med. Sc., Jan., 1910; Surg., Gynec. and Obst. Nov., 1918; Med. Rec., Dec. 26, 1914; Jour. Med. Res., Nov., 1914, XXXI; Am. Jour. Med. Sc., Feb., 1915; Arch. of Diagnosis, Oct., 1915; Am. Jour. Med. Sc., Sept., 1917; New York Med. Jour., Mar. 13, 1920.

³ For the application of Capillary Microscopy, see Chap. CVI et seq.

true vasomotor phenomena of transitory nature, such as alternating syncope, rubor and coldness, apparently independent of these chronic changes that have been cited above and that are distinctly traceable to the occluded condition of the arteries and veins; (4) the symptoms of pain, either in the form of intermittent claudication (pain in the calf of the leg or in the foot on walking with cessation when the limb is at rest) or the severe pain that is associated with the advent of trophic disturbances, especially with ulcers and patches of gangrene; (5) the slow course of the disease, symptoms of intermittent claudication or pain, preceding the development of trophic disturbances for months and years; (6) the fact that more than 95 per cent of the cases occur in Polish, Galician, or Russian Hebrews, and that almost always young males between the ages of 20 and 30 are affected with this disease; (7) the common onset of symptoms in the lower extremities, one of the legs being usually first affected; (8) the comparative infrequency of involvement of the upper extremities; (9) the association of a peculiar type of migrating phlebitis in the territory of the external or internal saphenous, less frequently in the larger veins of the upper extremities characteristic in about 20 per cent of the cases, and sometimes antedating the subjective and visually objective signs in the legs; (10) the slow but steadily progressive course, leading in a large majority of the cases to amputation of at least one limb, not infrequently of both lower extremities, and in rarer instances to amputation of one of the upper extremities as well.

Even a rapid review of the salient symptoms of thrombo-angiitis obliterans would seem to suffice to leave the impression that it could hardly be mistaken for other diseases. And were it not for the fact that certain symptoms closely resembling typical vasomotor phenomena may persist for weeks and years in this disease, confusion with the true neurogenic vasomotor processes would scarcely ever arise. The chronic condition of redness in thrombo-angiitis obliterans can be explained as due to dilatation of the superficial capillaries, this being a compensatory phenomenon making for an adjustment of the impaired circulation. This chronic redness or rubor may be mistaken for erythromelalgia or for the rubor of Raynaud's disease. The fact that it is associated with other evidences of closed vessels and the other characteristic features above mentioned together with the circumstances that the redness disappears at once upon elevating the extremity, will make the recognition of its nature possible.

In addition to this more or less chronic or permanent sign of deranged vasoconstriction, other phenomena which are truly vasomotor in nature may frequently be associated in thrombo-angiitis obliterans, and it is these that must be differentiated from similar phenomena accompanying Raynaud's disease, erythromelalgia, scleroderma, sclerodactyly, and acrocyanosis.

If we do not overestimate the importance of single manifestations of vasomotor irritation, but regard as more significant the clinical course and the symptoms in their totality, we will not fail to separate very clearly in our minds the true vasomotor phenomena.

It is true that there are still some who cling tenaciously to the theory that some lesions of the peripheral arteries may account for the symptoms of Raynaud's disease. In support of this view certain anatomical findings have been cited as strong arguments by those who believe that a definite anatomical lesion in the peripheral vessels is irresistible testimony against pure hypothesis. A careful analysis of the cases in question, as made by Cassirer, shows that reported organic alterations in the vessels will not suffice to explain the symptoms any more satisfactorily than the theory of a central nerve affection

of the sympathetic system. Whereas in thrombo-angiitis obliterans the territory manifesting symptoms corresponds to that containing the diseased vessels, we find that no such relation exists where vascular lesions are associated with Raynaud's disease.

For the clinical diagnosis of thrombo-angiitis we must depend upon (1) the racial (Hebrew) and sex (male) predilection; (2) the early involvement of the lower extremities; (3) the early symptoms of pain or intermittent claudication; (4) the presence of migrating phlebitis; (5) the evidences of pulseless vessels; (6) the presence of blanching of the extremity in the elevated position; (7) the existence of rubor in the dependent position; (8) the relation of the hyperemic phenomena to posture; (9) the absence of simultaneous, symmetrical involvement, and (10) the slow, progressive chronic course terminating in gangrene.

Whereas in thrombo-angiitis obliterans a definite and specific morphological change in the arteries and veins is responsible for the varied phenomena in the superficial capillaries, in Raynaud's and allied diseases the vasomotor and trophic disturbances are the outcome of irritative and exhaustive processes of the sympathetic nervous system.

Furthermore, characteristic for Raynaud's is the osseous atrophy and the striking absorption and disappearance of the terminal phalanges, well demonstrated by Roentgen ray examination.

2. From *organic arterial diseases* in general, the following differential signs characteristic of obliterated arteries should be sought for by a thorough clinical examination. When these can be elicited, Raynaud's syndrome can be excluded. They are:

(a) The symptoms of intermittent claudication, which is a clinical entity but accompanies occluded arteries of the lower or upper extremities from numerous causes.

(b) Coldness of the extremity, particularly influenced by climatic conditions, occurring spontaneously or brought on by exertion.

(c) Cyanosis or a bluish discoloration of the tips of the toes particularly the great toe, sometimes the ball of the foot, attended with coldness and particularly noticed after walking and in cold weather.

(d) Ischemia or blanched condition. Whiteness or a blanched condition of the extremity, occurring when the limb is in the horizontal, rarely even in the dependent position, and which can be elicited on examination by elevating the affected limb 60° to 90° above the horizontal (also known as ischemia).

(e) Redness or rubor. A condition of redness or rubor, involving the toes, sometimes the dorsum and the plantar aspects of the foot for varying distances to the ankle or even higher, frequently involving the lower extremities when these are allowed to hang down, occasionally occurring even in the horizontal position of the limb, and independent of infection, gangrene, or trophic disorder. The author has termed this phenomenon "erythromelia."

(f) Absence of pulsation. Absence of pulsation in the usually palpable vessels of the extremities, the dorsalis pedis, posterior tibial, popliteal or femoral of the lower extremity, the radial, ulnar and brachial arteries of the upper extremity.

(g) Trophic disorders including indolent fissures, ulcers, hemorrhagic areas, superficial ulcers, perforating ulcers, a withered or atrophic condition of portions of the extremity, foot or hand, impaired growth of nails, etc.

(h) Thrombosis. Attacks of thrombosis with the following symptoms referable to the sudden closure of vessels: Pain in the calf of the leg or in the foot, inability to walk, coldness, blanching of the foot on elevation, loss of

pulsation in the dorsalis pedis, posterior tibial or popliteal arteries, or all of these, sometimes followed by development of trophic disturbances, and even gangrene, or at other times eventuating in more or less complete recovery.

Treatment.—Unfortunately we have very little to offer in the way of therapy in this disease, since our knowledge of the etiology and pathogenesis is so meager. Our first care should be towards the attainment of improvement in the neuropathic diathesis, according to the well established rules laid down in Chap. CV.

Monro points out that since the vasomotor centers have the tendency to act with abnormal readiness in this malady, measures should be adopted to avoid everything that favors the occurrence of the individual paroxysms; and that the patient should learn to escape the conditions predisposing to an attack. Thus every precaution should be taken to avoid under exposure.

Not only should the feet be well clothed at all times, but gloves should be worn without causing the slightest interference with the circulation of the hands. In the worst cases it may be expedient for the afflicted to remain indoors in cold weather, with the room temperature kept warm at all times.

The application of electricity has been much vaunted as of exceptional value. Although a beneficial effect is occasionally obtainable, this measure has on the whole been found disappointing. Galvanic hand and foot baths of 10 minutes' duration are recommended by some authors.

One broad electrode as cathode is placed against the nape of the neck, the second, or anode, is placed in luke warm water in which one or both hands or feet are immersed. The current strength is regulated so that distinct prickling is experienced, the séances lasting at least 10 minutes. Both pain and vasomotor symptoms may be beneficially influenced by such application.

Good results are reported with the method of stasis or hyperemia suggested by Cushing, and applied by means of an elastic bandage. An ordinary muslin "ideal" (semielastic woven bandage) or rubber bandage is made to compress the upper arm until distinct venous stasis ensues, without, however, interfering with the arterial supply. A good result can often be observed, although occasionally the pain is intensified.

For the pain, rest with elevation of the affected parts and the usual coal-tar sedatives may be tried. Pyramidon, even more than antipyrin and phenacetin, seems to enjoy a favorable reputation. At times one will have to resort to morphine, although opium in other forms should be given a prior trial.

Little is to be expected of the vasodilating remedies. Both amyl nitrite and nitroglycerine have been found wanting, although beneficial in certain cases. Pilocarpine is believed by Hoesslin¹ to give temporary relief.

Arsenic perhaps is the best internal medication at our disposal, administered per os in the form of Fowlers' solution, or as sodium cacodylate hypodermatically. Papaverin recommended by Pal subcutaneously or intravenously as a vasoparalytic agent may be given a trial. Papaverin hydrochlorid is non-toxic, and may be administered in 0.03 to 0.08 gm. doses per os or subcutaneously, or 0.01 to 0.02 gm. intravenously.

Thyroid extract has been recommended by some; adrenal extract by others.

In a case of Raynaud complex attributable to pituitary disease, the administration of this gland was followed by considerable improvement in

¹ Hoesslin, München. med. Wchnschr., 1910, 29.

the symptoms.¹ It is, therefore, important to establish whether an endocrine deficiency is present in any given case, and to administer the corresponding endocrine abstract.

The operation of periarterial sympathectomy or arterial decortication is recommended by some of the French authors (Leriche²). Its value in this disease, however, has not as yet been satisfactorily demonstrated.

CHAPTER C

SCLERODERMA

It is because of the almost imperceptible gradations from one type to another occasionally presented by the obstructive and vasomotor clinical syndromes—morbid processes of wholly diverse pathogenesis—that it becomes necessary for the student of the circulatory disturbance of the extremities to include in the scope of his differential investigations a knowledge of the disease known as "Scleroderma." Whilst indurative tegumental disorders are *par excellence* the manifestations of this disease, almost identical objective alterations are seen in the Raynaud complex and are occasionally associated with thrombo-angiitis obliterans.

Mention has already been made in the chapter on thrombo-angiitis obliterans of the cases with marked sclerodermal changes in the upper extremities, and how the dorsum of the feet and lower part of the legs not infrequently show extensive indurative thickenings. But it is Raynaud's disease with its not uncommon coexistent signs of hardening of the integument that has most often been brought into association with sclerodactyly.

Most important of all, however, for differential diagnosis is the circumstance that vasomotor symptoms, such as local cyanosis, may precede by months or years the fully developed and characteristic picture of sclerodactyly. These are the striking clinical facts that warrant an examination into the salient features of this interesting malady in a work apparently devoted to another theme.

The literature abounds with appellations descriptive of the cutaneous scleroses—also known as dermatoscleroses. Most of these clinical complexes are now regarded as having a similar pathogenesis. Except for the condition *sclerema neonatorum* (sclerema of the newborn) the oft separately classified affection of *scleroderma*, *chronic progressive scleroderma*, *localized dermatosclerosis*, *morphæa* and *sclerodactyly* are best grouped under one inclusive term, namely, *scleroderma*. Since *sclerema neonatorum* is still regarded by a fairly large number of authors as being a distinct entity, attention will be focused on the other forms of dermatosclerosis which have certain features in common and which vary only in combinations of symptoms and their appearance.

The following forms have been described: first, a circumscribed form or *morphæa*; second, a chronic progressive form or *scleroderma*; and third, a subordinate form of the latter termed *sclerodactyly*.

Other descriptive appellations, such as *scleroderma diffusa* and those describing the limited forms, namely, *scleroderma en plaques* and *en bandes*, are found in the French literature.

¹ Pribram, München. med. Wchnschr., 1920, 67, 1284.

² Leriche, Soc. méd. des Hôpitaux de Lyon, Dec. 2, 1919; Lyon méd., Jan. 10, 1920, 40.

Symptomatology.—The cutaneous alterations have been divided into those of the first, or *edematous stage*; second, *the indurative stage*; and third, *the atrophic stage*.

First, in the edematous stage the skin presents a hard edema, with a smooth cutaneous surface. This change may be localized to small areas, may be transitory, coming and going, or continuously present. Sometimes it is of patchy nature or diffuse, or it may involve a whole extremity. It may be limited to one or another toe, to part of the lower extremity, to the hand, or even the eyelids. Gangrene of a toe is said to have followed this edema.¹

In the second, or indurative stage of the disease, the skin becomes hard, tense and stretched, often bound down, glistening, sometimes having almost a varnished appearance. By virtue of this change, the consistency of the skin becomes progressively harder, almost cartilaginous, board-like, and sometimes described as being even stony hard. It has been reported as encasing the body (*en cuirasse*). When the face is involved, it gives a typical mask-like appearance.

While at first there seems to be thickening, in a consequent stage attenuation may take place, so that the integument is thinner than normal. In this way depressions are produced. In both of the two latter periods of alteration, the skin is bound down, and cannot be displaced.

The areas involved may begin as small spots, or areas of pigmentation. Such have been described as having a reddish center, surrounded by a brownish red ring, the whole becoming indurated and prominent. Patches of whitish or violet color have been described.

The disease may begin acutely, within a few days or weeks, developing rapidly in intensity and extent, or it may take a slow course, in which case manifestations take years to become well marked.

The varied phenomena described by many authors as modifying the picture of scleroderma may be grouped under the following heads: first, disturbances in pigmentation; second, secretory changes; third, deranged vasomotility; fourth, trophic disorders; fifth, sensory disturbances; and sixth, disturbed motility.

First, the pigmentation. Lewin-Heller² in their study of the literature report a brownish or yellowish white color change to be most frequently observed. A grayish color, too, is not uncommon. Such pigmentation is found in the form of stripes or patches, or may be diffuse in the sclerodermal as well as in other parts of the skin. Even the mucous membrane may show pigmentation. In some cases a combination of Addison's disease and scleroderma has been observed. An absence of pigment has been described.

Second, the secretory changes. Either a general hyperhidrosis or increased sweating in the neighborhood of the sclerodermal skin is often a feature. But more frequently the affected parts show absent or diminished secretion of sweat. Probably the differences in reports depend upon the stage of the disease in which secretory activities were studied. Nerve influences are not unimportant in the determination of the activity of sweat secretion.

Notes regarding the activity of the sebaceous glands have been made by some authors, and the glistening shiny appearance of the skin in some cases is regarded as an evidence of undisturbed or even overactive sebaceous gland cells. The opposite effects, however, follow necessarily when through atrophy the glands are implicated, and their activity ceases.

¹ Legroux, *Gaz. d. hôp.*, 1880, p. 703.

² Lewin-Heller, *Die Sklerodermie*, Berlin, 1895.

Third, vasomotor disturbances. Local asphyxia or local syncope may be present for months or years before the symptoms of scleroderma manifest themselves. In the chapter on Raynaud's disease we have referred to the cases of sclerodactyly—a form of scleroderma—in which the vasomotor symptoms are prodromal manifestations. Later, because of the combination of symptoms of scleroderma and disturbed vasomotor innervation, the diagnosis may be difficult.

Many authors, however, have called attention to cases of true scleroderma in which there was a previous history of excessive reaction to cold in the form of asphyxia or local syncope. Indeed, in one case a cyanotic discoloration and swelling of the fingers (Thibierge¹) existed for 7 years.

In contradistinction to the asphyxia and syncope, other cases are reported as manifesting an active hyperemia, or such rubor associated with sensory symptoms. Thus, when rubor or painful paresthesia exists, a symptom-complex of the erythromelalgia type is present. The rubor may be diffuse, or appear in isolated patches; when of the latter type, it is particularly prone to be located near the joints.

The so-called lilac ring that is said to surround the patchy scleroderma (morphoea) has also been explained as being of vasomotor origin.

Regarding excessive response of the skin to external stimuli (dermatographism²) Cassirer does not agree with other authors, who in describing the occurrence of urticaria in this disease would also emphasize an increased vasomotor cutaneous irritability.

Possibly as manifestation of the disturbed vasomotor mechanism may be recorded the reduction of temperature of the part. Such obtains during attacks of syncope and cyanosis, but not in those of rubor. So, too, lowered temperature is noticed in the stage of atrophy.

Fourth, the trophic disturbances. In addition to the characteristic skin alterations above described, we may mention the following: trophic ulcers, nutritive changes in the skin, such as marked desquamation and hemorrhages; or, of the adnexa of the skin in the form of alterations in the hair growth and changes in the nails.

Of importance in differential diagnosis is the observation that ulcers occur especially at those bony prominences over which the skin is already sclerodermatic or atrophied. They may, however, have a precocious development and appear in places that are not as yet subject to the specific alterations. Indeed, they may precede by months or years the advent of the typical phenomenon. Hardy³ describes the occurrence of pustules or vesicles leading to the formation of superficial ulcers, then healing and the formation of superficial scars. Or, there may be very deep-seated ulcers destroying the skin and deeper tissue, and even with gangrene of small areas or territories.

Indeed, *gangrene* has been frequently reported as complicating cases of scleroderma. Foulerton⁴ observed a gangrenous patch on the dorsum of the foot, another over the internal condyle of one of the legs necessitating amputation. Cassirer reports a case of painful gangrenous ulcer of a finger with sequestration of a piece of bone. He believes that ulcers may occur spontaneously without previous vesicle formation, in that there develops a crust confining purulent fluid. The formation of ulcers is regularly attended with pain. Sometimes the ulcers are symmetrically situated.

¹ Thibierge, Soc. d. Dermat. et Syph., 1905, XII, 7.

² See chapter on Vasomotor Innervation of the Skin.

³ Hardy, Gaz. d. hôp., 1877; also 1881, p. 97.

⁴ Foulerton, Lancet, 1892, XI, 12.

The disorders in the adnexa of the skin are especially disturbed hair growth. Most marked in the sclerodermal areas, does the hair become friable, thin, dry, and often of a bristle-like appearance. Or, there may be complete loss of hair over the whole body, the alopecia sometimes antedating the sclerodermal symptoms.

The nails may become furrowed, easily broken, deformed, hook-like or crooked, may show membranous covering, or there may be atrophic conditions with degeneration of the nails into tiny platelets that may wholly disappear. Even the teeth are said to fall out spontaneously and the gingival mucous membranes atrophy.

Fifth, sensory disturbances. In contradistinction to the Raynaud complex, scleroderma may be unattended with subjective sensory disorders, and may run its course without any pain whatsoever. According to the statistics of Lewin-Heller all sensory changes were absent in a large number of the cases examined. Thus, Cassirer noticed the existence of paresthesiæ, burning sensations, itching, a dull feeling of numbness, or a sensation as if the part were asleep, often in the prodromal stage. Or, with paresthesia there may be attendant pain of tearing, sticking or burning nature. Or, there may be a feeling of tension in the skin that calls the attention of the patient to the cutaneous alteration. The pain may last for years, and is usually diffuse, not localized within the distribution of any nerve.

Another evidence of sensory disturbance is the excessive reaction to cold, which may be so intense that the patients are unable to touch a metallic object, even a door-knob, for fear of exciting painful sensations. The sensibility may remain intact. However for the most part the sensory disturbances are not constant, may be absent, and the subjective sensations are infrequent and usually not well marked. In most of the cases the local condition runs parallel with the sensory disturbances and explains these sufficiently.

Sixth, disturbed motility. Varying degrees of impairment of motion depend upon the situation of the scleroderma, the degree of involvement of the skin, and the implication of the deeper parts, the muscles and joints. Most striking of all is the immobility produced in the face through the cutaneous changes with the resultant changes known as the *sclerodermal mask*. Not only is there a fixation of the facial muscles, but, when the pressure attains sufficient degree, difficulty in opening the mouth, deglutition and mastication may be the consequence.

So also, the interphalangeal joints may suffer becoming restricted in their excursions, and even fixed.

When the muscles are involved, it is not uncommon to find atrophy usually due to muscular inactivity. Because of the difficulty encountered in palpating through the indurated skin, it may be impossible to distinguish between lesions of disuse from atrophy due to compression of the vessels and nerves, or, from sclerosis of the muscles themselves. In sclerodactyly muscular changes occur very frequently. Myosclerosis with an indurative condition of the muscle fibers has been reported.

Complicating Lesions. Osseous Changes.—These may be both of the atrophic and hypertrophic variety, although the former is the more common and characteristic. Atrophy is especially noteworthy in the cases of sclerodactyly, in which shortening and rarification of the bones occur. Even without trophic disorders or ulcers or gangrene, a gradual and total resorption of the terminal portion of the phalanges, or a whole phalanx may develop; or, with the process less advanced, a narrowing and shortening of single

phalanges is noteworthy. This atrophy is well demonstrated in the Roentgenogram. Some authors describe an atrophic process of the long bones, with diminution in size and shortening of the arm bones.

A particular clinical picture designated as *acromicria* has been described in which diminution in the size of the terminal parts of the phalanges gives a remarkable appearance. Because of the disparity in the thickness of the base of the fingers and their terminal digits, a characteristic tapering is developed.

The rarefaction of the spongy bones may involve those (shoulder-blade) that are covered by normal skin. The reticular osseous structure may appear inordinately well marked in the X-ray pictures but the meshes are widened. Even foci of bone absorption have been noted.

The so-called hypertrophic processes in the bone are not true enlargements as a rule, but often represent ossified myositis, or merely osteophytes.

The Joint Lesions.—It has been noticed that rheumatic or articular conditions precede the development of scleroderma. Dercum describes a form of rheumatism, due in his opinion to secondary changes of a sclerotic nature. Ankylosing arthritis, fixation of the tarsal joints, implication of the interphalangeal articulations, and conditions similar to arthritis deformans are cited in the literature.

The Mucous Membrane.—The tongue is most frequently involved and immobility of the mucous membrane as also atrophy, ischemia, participation of the pharyngeal and gingival mucous membranes are amongst the various lesions seen in this region.

General Symptoms.—Most cases run a course without fever. Subacute febrile periods may develop with general malaise, insomnia, loss of appetite and diffuse pain. Blood examinations give varying findings, diminished red blood cells, increased eosinophiles or normal findings. There are frequently digestive disturbances, vomiting, constipation, sometimes diarrhoea, and nausea.

Albuminuria occurs frequently, glycosuria occasionally.

An important associated symptom is the enlargement of the thyroid occasionally seen, and sometimes sufficient to be regarded as Basedow.

Vasomotor symptoms may partake of the Raynaud or angiospastic type, and more rarely resemble the picture of erythromelalgia. In the chapter on Raynaud's Disease the occurrence and coexistence of the symptoms of the latter with sclerodactyly have been discussed.

The clinical complex in such cases comprises sclerodermal changes in the extremities, occasional attacks of local syncope, later ulceration and even gangrene.

But even in that form of sclerodermal affection known as *sclerodactyly*, vasomotor symptoms are apt to be prominent, consisting of local cyanosis, local anemia, and hyperemia. Or, there may be recognized special groups in which the vasomotor manifestations take the following form: firstly, in a manner indistinguishable from typical Raynaud's disease; secondly, with an onset consisting of local asphyxia and syncope, but without any progressive development into the typical Raynaud's complex, symmetrical gangrene being absent; and thirdly, with vasomotor symptoms following the sclerodermal changes.¹

Symptoms of Erythromelalgia.—Some authors have reported an association of symptoms of the three affections, erythromelalgia, Raynaud's

¹ (Chap. XCIX, Raynaud's disease with sclerodactyly.)

disease and scleroderma. Attacks of local asphyxia, patchy or diffuse scleroderma of the hands and feet, gangrene and pain, and periods of vascular dilatation over the hands—these complete a picture in which the signs of erythromelalgia are in evidence.

Clinical Course.—The phases characterizing the development of this disease have been variously described. Probably the most useful classification is that into (1) a neurotic or prodromal stage; (2) one of edema; and (3) that of induration and atrophy. Because the cutaneous alterations may advance with varying degree of rapidity in different types of cases, such distinctions are only valuable as descriptive of the stage in which the lesions are found. Indeed, it would be almost impossible to put a limit to the prodromal stage in which vasomotor symptoms with or without sensory disturbances may dominate the picture.

Then again, the cases have been grouped into acute or chronic, with innumerable transitions. The condition may last for many years, some authors reporting a protracted course. According to Lewin-Heller, there are instances with a duration of from 15 to 48 years.

The disease does not progress continuously. Long intervals of apparent arrest or localized cessation with appearance of new areas of cutaneous involvement elsewhere may occur. Improvement has been noted even to the restoration of typical sclerotic zones into almost normal skin. Indeed, even complete healing is possible. Pigmented areas may remain after regression of the symptoms.

Acute scleroderma develops occasionally in children, with well marked cutaneous changes elaborated within a few days, or a very few months. A chronic stage may supervene.

Pathogenesis.—Four theories have been advanced in explanation of the malady: (1) Malfunction of endocrine glands; (2) infectious agents; (3) vascular; and (4) neurotic factors.

Thyroid Imbalance.—Some believe that a primary disease of the thyroid gland is responsible for the elaboration of a toxin that produces the characteristic cutaneous changes. Indeed, it has been noted that scleroderma and Basedow may be associated. There does not seem to be much foundation for such a theory. Furthermore, the association of the two affections is not found in the majority of cases. Others suggest that both scleroderma and thyroid malfunction in Basedow's disease may depend upon or be due to disturbance of the central innervation of the vegetative nervous system, and that the latter produces the anomalous function of this gland. There does not seem to be enough data to warrant the assumption that thyroid disease is a primary cause of scleroderma.

As for the relation of the thyroid to the scleroderma, some authors are of the opinion that the malfunction of this gland in Basedow is rather the result of disturbances of innervation in the vegetative system, than of primary origin. In view of this assumption, whenever scleroderma and Basedow are associated, they refer again to the nervous system as the primary cause of the affection.

The theory of abnormalities of *internal secretions* has received some support and even a so-called pluriglandular insufficiency has been reported as responsible. To group it with Raynaud's and similar affections or with the lepra group is unwarranted. Insufficient evidence is at hand at the present time to permit us to seriously entertain such an hypothesis. The vascular theory has been put forth as an explanation on the basis that the terminal arteries or arterioles are diseased. Binkler describes a perimeso and endarteri-

tis chronica fibrosa, especially of the skin vessels. Even though it must be admitted that changes in the cutaneous vessels do occur, it would appear that these are rather attributable to a primary, more remote causal agent somewhere in the nervous system.

To the enlargement of the pituitary gland (Pribram¹) a causal influence has been attributed.

The nerve theory finds its adherents who designate variously the central nervous system, the peripheral, or the sympathetic, either in an anatomic or a functional sense, as the cause of the malady. Lewin-Heller interprets the symptoms of scleroderma as due to disease of the vasomotor and trophic centers and paths; and since the anatomic basis for such an assumption has not as yet been satisfactorily discovered, the disease has been regarded by him as a vasomotor trophic neurosis, or an angio-trophoneurosis.

The *vascular* theory can be rejected for it has never been proven to be present in advance of the sclerodermal changes; nor are there parallel or analogous alterations following arterial disease due to other causes. Nor could we explain by the vascular theory, the intermittent course of the malady, nor the sensory disturbances and other trophic derangements that occur here.

Rather important confirmatory evidence in favor of the *neurogenic theory* is the close relationship between scleroderma and Raynaud's disease and other vasomotor trophic neuroses. Indeed, the asphyctic symptoms, and the local syncope not infrequently form a part of the symptom-complex in scleroderma, these manifestations, as before noted, preceding sometimes for months or even years with the appearance of typical trophic symptoms. Therefore, these diseases are intimately related, and both would seem to have a neuropathic origin.

As for the nature and the locality of the lesions of the *nervous system*, little except hypothesis can be offered. Perhaps there are multiple motivating factors. But, as far as we know today, gross changes in the nervous system have not been found to account for the symptom-complex of the malady. We know that destruction of the higher vasomotor centers, namely, those parts that control the trophic functions of the tissues, does not produce scleroderma. As evidence we have the cases of transverse lesions of the spinal cord; and even in gliosis, where there is long continued irritation through the proliferation of the glia tissue, severe intense trophic changes are observed, but not of the scleroderma type.

Cassirer assumes that there is some sort of irritation of the higher centers which the subordinate centers cannot inhibit or control, and that this stimulus is brought about by varied moments, infection, exogenic and endogenic intoxication, and reflexes.

Diagnosis.—This is usually simple as soon as the characteristic cutaneous changes are developed. The early stages of the disease, however, particularly when abnormal localization occurs, may give rise to some difficulty of recognition. These are the patients in whom the mucous membrane, the subcutaneous tissues, the bones, muscles and joints seem to manifest the first alterations.

In some cases the onset can be mistaken for the acroparesthesiæ. So, too, local asphyxia and syncope may precede the development of the typical picture, and we have elsewhere referred to the similarity between the Raynaud and scleroderma complex.

¹ Pribram, Deutsch. med. Wchnschr., 1920, 46, 87.

In the persistent edemas (after cold, erysipelas, etc.), the consequent induration of the skin is but slight in comparison to that found in scleroderma, and atrophy does not occur. We have elsewhere alluded to the indurated edema, associated with spinal cord lesions (myelitis).¹

In a case reported by Thibierge and Boutelier² there was associated edema that gave a picture simulating scleroderma.

For the cutaneous phenomena of dystrophic nature occasionally observed in thrombo-angiitis, the reader is referred to Chap. LIX.

Idiopathic Atrophy of the Skin (Erythromelie³).—Under this caption symptom-complexes have been described in which cutaneous atrophy is characteristic.

Pick suggested the name "Erythromelie," Buchwald "idiopathic diffuse atrophy," Herxheimer "acrodermatitis atrophicans chronica progressiva" and "dermatitis atrophicans maculosa."

The disease usually begins with the formation of red or bluish red patches suggesting an inflammatory erythema, stasis, or passive hyperemia. These become larger and confluent until a large area of the skin is involved. Soon, an abnormal flaccidity or relaxation of the skin develops, with folding of the superficial layers; and an appearance of crumpled tissue paper becomes characteristic. Wherever displaceable skin is normally present, as over the back of the hand, knee and elbows, this plication is particularly accentuated. The skin becomes dry, adipose tissue reduced and the hair falls out. The vessels shine through with abnormal prominence in network-like fashion. Usually the affection is symmetrical over the extremities, the extensor surfaces being more intensively involved. Sensory disturbances are absent or very slight, there being no objective derangements of sensation, although slight pain may be present.

Some French authors describe the skin of the affected region as showing a curious picture of atrophy and infiltration of apparently inflammatory nature, with an admixture of red and blue color as the striking phenomenon. The terminal portions of the extremities seem to suffer the maximum alteration, especially where the integument is almost in contact with the bony planes (elbows, knuckles, etc.). The affection develops chronically and usually attacks men between the ages of 30 and 50. In short, it is a sort of premature cutaneous degeneration.

Various theories have been proposed in explanation of the malady. Some regard it as an anomaly of development; others attribute it to vasomotor lesions; and others accept a fundamental endocrine dyscrasia.

Prognosis.—Although the type known as scleroderma proper often shows a tendency to improvement or healing, sclerodactyly is less apt to take this course. A cure is most likely to occur in the acute cases, and in general, it is stated that the prognosis is better in children where almost 30 per cent are believed to lose their manifestations. Improvement is reported by Lewin-Heller in about 30 per cent.

A lethal outcome is very rare; but in severe cases, a sort of cachexia has been observed. The localization of the process has a bearing on the physical state. Impairment of mastication may make feeding difficult; or restraint of respiration through implication of the chest wall is an eventuality to be feared. Such are complications that impair longevity.

Therapy.—We possess no drug that seems to specifically influence this malady. Where healing takes place, it cannot be attributed to the drugs given. Thyroid extract and thyroïdin have received most recommendation. Their value is, however, rather doubtful; they certainly are not specific. Other internal secretions as that of the adrenal have failed. Salol and salicylic preparations have been suggested and regarded as of some value by certain authors. Various forms of electric therapy also, electrolysis, elec-

¹ See Trophic Lesions in Chap. LXXXIX.

² Thibierge and Boutelier, Soc. Fr. de Dermat. et Syphiligraphie, 1920, 27.

³ Note that the appellation *Erythromelia*, as used by the author is not to be confounded with the German "Erythromelie" (Pick) found in German literature.

tric baths, have been much vaunted by some authors. Massage is of some value in increasing the suppleness of the skin, and overcoming the atrophy of inactivity, as also are hydrotherapeutic measures. Hot air treatment also has found its adherents, injection of thiosinamin (50 per cent alcoholic solution), or fibrolysin, none of which, however, seem to have met expectations. Improvement of the general health seems to do as much as any drug for the condition.

CHAPTER CI

MULTIPLE NEUROTIC GANGRENE

There are observations in the literature on the occurrence of multiple gangrenous lesions of the skin that are not attributable either to changes in the vascular system, to alterations in the general nutritive condition of the patient, or to bacterial invasion. In most of the cases there were stigmata of nerve disease. The cases vary considerably in detail, so that a typical picture cannot be described.

The large number of names suggested is in keeping with the variability of the symptomatology. They are acute *multiple gangrene* of the skin (Dinkler,¹ Zieler²); *multiple trophoneurotic gangrene* (Müller³); *multiple neurotic skin gangrene* (Kopp,⁴ Joseph,⁵ Adrian⁶); also *spontaneous skin gangrene* (Cronequist and Bjerre⁷); *multiple insular necrosis of skin* and subjacent tissue (Renshaw⁸).

In spite of the fact that many of the reported cases are artificial and occur in hysterical individuals, there remain some of undoubted authenticity; in these multiple neurotic, non-artificial gangrene occurs. Here belong the cases of Kopp, Hinter, Joseph, Doutrelepont, Singer, W. Sinkler, Neumann, Leloir, Renaut, Zieler, Kreibich and Bronson.

Etiology.—Of twenty-five examples studied by Cassirer three were males; all were young individuals; eleven between the ages of twenty to twenty-seven; thirteen from eighteen to twenty years.

Two factors, trauma and a neuropathic predisposition are seemingly essential for the production of the symptom-complex. In seventeen of the twenty-five cases, trauma is reported, and seven times a burn of the second degree.

Such burns were noted seven times in a total of twenty-five cases. It would seem that through some agencies hypersensitiveness of nerves is brought about. That the history of previous burns is not merely coincidental is attested by the large percentage of previous mechanical and thermic insults. Furthermore the intimate relationship between the locality of the gangrene and the previous injury is noteworthy. Often the site of necroses

¹ Dinkler, Arch. f. Dermat. u. Syphil., Bd. LXXI, S. 61.

² Zieler, Deutsch. Ztschrft. f. Nervenhe., XXVIII, S. 184.

³ Müller, Centralbl. f. inn. Med., Wiesbaden, 1902, S. 521.

⁴ Kopp, München. med. Wchnschr., 1886, S. 665.

⁵ Joseph, Arch. f. Dermat. u. Syphil., XXXI, S. 323.

⁶ Adrian, Deutsch. med. Wchnschr., 1902, S. 143.

⁷ Cronequist and Bjerre, Arch. f. Dermat. u. Syphil., CIII, S. 163.

⁸ Renshaw, Brit. Med. Jour., 1894, I, p. 1238.

is confined to the side of the injury. In some cases the gangrene appeared a few days after the trauma, in others four to six weeks, and in still others many months or more than a year, in which case there could hardly be any relationship between the two.

In a large percentage of the patients a diagnosis of hysteria could be made. In others the symptoms of general neurosis were present. However, the material at hand is not adequate to warrant the view that multiple gangrene is always a hysterical affection, although in the majority of instances neurotic stigmata are present. Multiple gangrenous foci have been observed in the territory in which motor and sensory disturbances of spinal gliosis occurred. In peripheral neuritis, other authors (Neuberger¹) report gangrenous areas of the skin.

Where the lesions resemble a toxic urticaria, one would have reason to doubt the validity of the neurogenic theory of causation. Many of the other cases, however, because of the presence of a marked neuropathic diathesis and hysterical habitus, suggest a correlation between the two conditions. However, since this form of gangrene accompanies but very few instances of hysteria, the latter must be regarded rather as a predisposing factor than a causal one.

An attempt has been made to explain the influence of the previous trauma as a causal factor. Wherever injury was noted, it would seem that a prolonged irritation on the peripheral nerve ending was present. Such stimuli warrant the assumption that an increased irritability of distant vasomotor paths was thereby produced in a reflex fashion—in territories already labile by reason of the neuropathic disposition.

Organic changes in the nervous system were not found in the one case in which an autopsy was performed.

Symptomatology.—The most characteristic symptom is the appearance of multiple small necrotic areas in the skin without any alteration in the general condition to account for these, without any local bacterial infection, and without vascular lesions.

Preceding the appearance of gangrene, burning and pricking sensations are experienced in the corresponding skin areas. Sometimes these sensations occur as prodromal signs preceding the latter by a few minutes, hours, or days. Or, an anesthetic sensation or itching and even pain in the vertebral region at the level of the lesion may antedate the onset.

The sensory or irritative symptoms are not constant, and do not always accompany the advent of all of the necroses in any given case. At times the pains are very severe, or there are diffuse aches in the affected limb.

Vasomotor symptoms are rare. In one case there was a large patch of urticaria, which became hyperemic, then hemorrhagic and finally showed a black spot in its center. This spot became gradually larger to about 3 mm. in diameter, and after twelve days began to sequestrate. The other necroses were of larger dimension. In the case reported by Truffi² severe pain was followed by pallor in the skin, with the development of an edematous glistening area surrounded by a red zone.

Some cases are reported as being preceded by the formation of blebs. According to Leloir formication is followed by the appearance of a red spot of varying size in the skin. After some hours a greyish white patch with a red surrounding zone develops in its center. After several hours there is a central depressed area that becomes yellowish, then darker until finally it is

¹ Neuberger, *Deutsch. med. Wchnschr.*, Nov. 20, 1902, *Vereinsbeilag.*, p. 28, 1903.

² Truffi, *Rev. de méd.*, 1904, p. 992.

blackish and gangrenous, the total duration of the process being from thirty to forty-eight hours. Doutrelepont¹ observed first hemorrhagic redness attended with burning and prickling followed by the formation of a yellowish spot. Other authors speak of the origin of gangrene in coalescing vesicles.

The result of the various lesions described by numerous authors is a slough of varying appearance. It has been described as yellowish white, grayish, greenish gray, sometimes soft, other times dry and hard, and parchment-like. The size of the affected area is also variable (1 × 4 cm.), associated with spots the size of a lentil, 3 mm. in diameter up to the size of a dollar, or even larger. The necrotic area may be so hard that it cannot be penetrated with a pin or needle. Later an inflammatory zone usually appears about the slough. The defect after separation is usually superficial, rarely involving the subcutis. In one case, however, the mortification reached as far as the musculature (Hintner). The time required for the separation of the sloughs varies, the cicatrizing process being a slow one, taking from days to weeks and even months (4-5 months). Keloid formation is frequent.

The mucous membranes, too may show lesions, though rarely. Necrosis in the throat, genitals, conjunctiva, mouth and tongue are reported. In one case there was first a vesicular eruption of the lower lip, and two months later a gangrenous vesicle in the territory supplied by the left trigeminal nerve. Two years later a gangrenous patch appeared in the neck, then over the upper arm, breast, upper lip and auditory canal.

Clinical Course.—A nervous patient gives a previous history of trauma, after which either in the original scar, or in its vicinity, the first gangrenous patch appears. When the lesions are multiple, the youngest lesions are usually found proximal to the original one, so that various stages in the process can be recognized from above downward or from the center towards the periphery. The process may be limited to one side of the body, or after months may involve the other side. The cases of Truffi and Kreibich are typical, where both sides were involved but not synchronously.

In the severe cases the lesions may be disseminated over the whole body. Even the external auditory meatus and the ear-drum may be affected.

The necroses may occur in rapid sequence and over considerable periods of time (3 years), during which there may be an almost continuous reappearance of necrotic areas. In one case (Sinkler²) this period was 7 years, during the first 4 of which the left arm was affected, and later the right forearm. In the case of Truffi, the duration was about 17 years. In some cases the intermittence may be greater from several months to years. Therefore, the course is not unlike that described by Kaposi in his *herpes zoster gangraenosa hysterica*, in which the duration was from 10-20 years, with free intervals of weeks and months.

Prognosis.—This is favorable as to life expectancy. As for duration, however, a prolonged period may be expected, with constant reappearance of gangrenous plaques.

Pathogenesis.—Multiple neurotic gangrene cannot be regarded as a disease *sui generis*, but rather as a symptom-complex. In most of the cases it would appear that changes in the nervous system could be held responsible for the necroses. There may, however, be a form of multiple gangrene due to multiple arteriosclerotic disease of the skin vessels (Cassirer). Even the

¹ Doutrelepont, Arch. f. Dermat. u. Syph., 1886, S. 179.

² Sinkler, Jour. Nerv. and Ment. Dis., 1897, p. 11.

true neurogenic forms are not of uniform nature. The process may be a rare symptom of organic nerve disease, such as spinal gliosis, tabes, peripheral neuritis and herpes zoster. Where necrosis is associated, we may speak of the lesion as *urticaria gangraenosa*. There is a marked hysterical habitus present in other cases.

Diagnosis.—It is important in establishing a diagnosis to exclude the cases of malingering and artificial hysterical traumata.

Thus, caustic soda has been known to have been employed artificially for the production of lesions by hysterical individuals. In the case of Strümpell, such was the case, but a marked dermatitis antedated the necrosis. Other caustics—such as zinc, chloride, sulphuric acid, cantharides, hydrochloric acid, and croton oil—have been similarly employed.

As a differential point between artificial and spontaneous skin gangrene it has been suggested that in the spontaneous form, the necrotic, deeper portions of the skin can be seen through the superficial bleb. Furthermore, when the necroses appear in situations that are inaccessible to the manipulations of the patient, their spontaneous nature is thereby made apparent. Variability of the lesions, the polymorphic nature of the necroses, their irregularity in limitation—all these speak for artificial products. And furthermore, if they cease to appear, when the patient is under careful observation in the hospital, they are usually the result of malingering.

The excision of pieces for microscopic examination (Zieler) has demonstrated that no destructive influences acting upon the surface can be noted. In the chemical necroses, the changes in the papillæ are reactive in nature, and secondary to the external irritation, with very few or no changes in the deeper layers.

It is well to search for organic nerve lesions in all cases, amongst these particularly spinal gliosis, tabes, and disease of the peripheral nerves.

There is another form of multiple gangrene, which has no relation to the nervous system, but is an expression of a *general cachexia*. In addition to the latter symptom of asthenia, there are usually present the following manifestations: fever (which is absent in multiple neurotic gangrene), variability in the extent of the gangrene, and the rather restricted course, there being a more sudden development than in the multiple neurotic type.

Therapy.—Arsenic, iron, calcium phosphate and potassium iodide have been recommended. Other authors have tried obstructive hyperemia with variable success.

CHAPTER CII

VASOMOTOR INSTABILITY

There are a multitude of variations in clinical pictures offered by vasomotor instability of the extremities.¹ The asphyctic symptoms may predominate; or the pallor or signs of angiospasm or a tendency to simulate erythromelalgia may be a feature. Where the manifestations are associated with walking, a resemblance with the vasomotor type of intermittent claudication is striking. But, if we accept the warranted conclusion that the large majority of so-called cases of intermittent claudication are attended with organic disease of the vessels, usually obstructive, there remain those

¹ See also Chaps. CVII et seq. for recent work on the vasoneuroses and the *vasoneurotic* constitution.

in which spinal cord vascular lesions are held responsible for the phenomena, and another type, in which true vasomotor symptoms seem to be evoked by muscular action. In some of the patients who make particular mention of the interdependence of symptoms and locomotion, close questioning demonstrates that such association is not at all essential, for symptoms may come on even when they are at rest.

We should never lose sight of that group in which sensory and vasomotor derangements are attributable to thermic influences, whenever exposure to cold has been excessive, and was followed by chilblains or freezing of a part. It has been already pointed out that it is not uncommon for various phenomena of such nature to supervene months or even years after the part was subjected to cold.

Vasoneurotic constitution is a term that has been applied to a condition characterized by instability of the vasomotor mechanism (Parrisius¹). Here alterations in vascular innervation manifest themselves either without apparent cause or after very slight provocation. Deviations in the caliber of capillaries occur over varied localities and in varying degrees at different times. Parrisius found that in the vasoneuroses the capillary loops at the base of the nails may evince remarkable differences in size, some being normal, others greatly dilated.

In the pronounced cases of vasomotor lability, local arterial spasm may be a striking manifestation. The following is an example of vasomotor instability:

Striking rubor in the horizontal position, occasional blanching of the big toe, occasional coldness and numbness on walking with pulsating vessels.

T. H. W., 36 years of age, American, asserted that his feet and hands always had a tendency to become bluish and reddish during the winter months (Dec. 3, 1912). One month ago his left leg became somewhat numb, and gave him some trouble on walking. He thinks that 2 weeks ago his left leg was decidedly numb, and rather cold. For the last 3 or 4 days the soles of the feet have been tender and there was pain in the left leg and thigh. Being a physician, he suspects that he has thrombo-angiitis obliterans.

On examination, Dec. 3, 1912, the feet are distinctly colder than normal, and have a tendency to remain cyanotic. All the vessels pulsate strongly, the symptoms being more pronounced on the left side. The chief manifestations are coldness, and numbness of both feet, particularly the left.

Diagnosis. Vasomotor neurosis.

The patient was again seen on March 1, 1915. Since he was last examined, he improved rapidly, and was almost free from symptoms until 6 months ago. At this time *redness* of both feet developed. This was particularly noticeable at night, and associated with some tenderness of the right foot. For the past 10 days the feet have been cold; both big toes have been markedly blanched. He stated that it required considerable rubbing to bring back the color.

The Wassermann test was repeatedly negative, the blood pressure normal, migrating phlebitis and intermittent claudication absent.

The chief symptoms, at the present time, therefore, are the numbness and coldness of the toes, the rubor at night and some weakness of the legs.

Physical examination, March 2, 1915. In the horizontal position both feet are redder than normal, particularly the toes. The left foot is slightly colder than the right, but more than normal at the surrounding temperature. The color changes and the redness are accentuated through fluctuations during the period of observation. In the dependent position the redness does not deepen. In fact, the right foot loses some of its color, but the dorsum becomes more purple owing to the distension of the veins. There is no increase of the redness in the dependent position. On elevation a decrease of the rubor ensues. The upper extremities, too, are markedly red, but without symptoms.

Conclusion.—A vasomotor case, the striking feature being the redness in the horizontal position, partly disappearing on elevation, but not completely: *No true erythromelalgia.*

In a communication received Sept. 25, 1922, the patient (a neurologist) says that the symptoms have completely disappeared, and he seems to regard them as having been of neurotic nature.

¹ For complete description of this complex see Chaps. CVII et seq.

Not infrequently the symptoms are attributed to exposure to cold although the influence of the latter cannot be accurately estimated.

Vasomotor neurosis in a young woman, chronic rubor, and swelling of the hands.

E. N., female aged 20 years, says her present condition has existed for nine years, was initiated by an attack of chilblains with both hands and toes frost-bitten. Her hands are always red, somewhat swollen and moist, especially in cold weather, and neither electricity nor organotherapy have been of any avail.

Physical examination (Dec. 23, 1919) revealed a somewhat nervous young woman, whose hands perspired profusely. The tips of her fingers were very cold, the whole of the hands puffy. When the fingers were compressed the return circulation was very sluggish. The lower extremities too were abnormally cold. The usual palpable vessels pulsated.

Vasomotor neurosis, chronic rubor, cyanosis and coldness of feet, especially in cold weather.

L. C., age 20 years, female, married (Jan. 18, 1918), says that her right foot was frost-bitten some seven years ago. Since then her feet have always been cold and red, especially in cold weather. There is no pain. Seven weeks ago the little and great toes became cyanotic. There is a drawing sensation over the dorsum of the right foot. (None of the symptoms of thrombo-angiitis obliterans are present.)

Physical examination reveals marked rubor of both feet, especially the right, whilst all the vessels pulsate normally. On leaving the limbs exposed for some ten minutes, they become somewhat cyanotic, the rubor diminishing. Ischemia on elevation is absent. Confirmatory examination one month later showed the same degree of rubor.

CHAPTER CIII

ATYPICAL VASOMOTOR NEUROSES

In this group we may include a variety of atypical affections in which the symptoms consist of merely vasomotor disturbances or those associated with trophoneuroses, the larger arteries being demonstrably patent; yet the clinical picture deviates considerably from the Raynaud complex or from erythromelalgia.¹

1. Localized Asphyxia with Arteries Pulsating.—Characteristic here are the *presence* of all the pulses, the absence of intermittent claudication, of ischemia on elevation, and even of reactionary rubor. This complex cannot be differentiated clinically from the type of thrombotic gangrene associated with healthy vessels described in Chap. XCVIII. Possibly an angiospastic stage precedes the syndrome discussed as “thrombotic peripheral gangrene” (although the histories do not suggest it); and superinduced by cold or other insult, a stage of chronic cyanosis with gangrene results, the peripheral thromboses being secondarily induced. Here, because of the transitory and often evanescent nature of the affection, the existence of a pure neurosis is most probable.

I. G., age 68, the little toe of the left foot had been cyanotic when she was admitted to the hospital in January, 1914. She had then complained of “sticking pain” in the toes for several weeks. On July 15, 1914, she returned with cyanotic discoloration of the adjacent toe, *the toe formerly affected being practically normal.*

Physical examination: The fourth toe of the left foot is deeply cyanotic and cold, the adjoining sole also bluish. The fifth toe is negative. Pressure over the discolored toe elicits pain. No ischemia on elevation, no rubor, none of the usual appearance of thrombo-angiitis obliterans or arteriosclerosis; all the arteries pulsate.

¹ For Capillary Microscopy in the Vasoneuroses see Chaps. CVI, CVII et seq.

On July 27, 1914, a red area seemed to be extending from the base of the fourth toe toward the tip, suggesting that cyanosis was disappearing, yielding to reactive hyperemia. No further observations could be made after July 28, since the patient left the hospital.

At first glance such cases might be mistaken for atypical Raynaud's disease or atypical localized acroasphyxia. But from the former, they are distinguished by the involvement of one toe at a time, the lack of symmetry, and the absence of paroxysmal attacks. From the latter affection there is even more marked deviation, both from the anesthetic and hypertrophic forms; the localization, the short duration, the absence of dystrophic processes stamp it at once as of wholly different nature. It properly belongs, therefore, to an *atypical* or *intermediary* group of vasomotor neurosis. The very limited distribution of the cyanosis and the pain and tenderness are in contrast with the more extensive cyanosis and the hypaesthesia of acrocyanosis.

2. Rubor and Cyanosis.—Color changes of the lower extremities with or without slight edema characterize certain cases of vasomotor instability where the vessels pulsate and there are no evidences of arterial obliteration. The feet and legs tend to become reddish, then cyanotic in the pendent position. They may be colder than normal, and a play of colors with a marmorated appearance of the skin of the foot and leg may occur from time to time.

A. G., female, age 19, dates her trouble back to an attack of erysipelas 6 months previously. She complains of having had some swelling of the feet even before this attack came on. Present complaint, discoloration and swelling of the legs with some pain along the inner aspect.

Examined after standing, both feet are quite *cyanotic*. This color gradually disappears in the horizontal position, being replaced by a marked mottling (*cutis marmorata*) that extends up to a short distance above the knees. After manipulating the legs incident to the examination, the *color of the left leg changes again, pinkish areas interspersed with cyanotic patches* making a striking contrast. These changes also arise when the legs are at rest. All of the vessels pulsate strongly.

3. Vasomotor Symptoms with Slight Trophic Disorders.—As vasomotor phenomena become associated with trophoneuroses, the cases approach erythromelalgia and Raynaud's syndrome, although there are still a number of intermediate forms which belong to neither of the two latter clinical entities.

Coldness, rubor, with ungual dystrophies and pain, especially nocturnal, make a picture not easily grouped with the well known and classical forms of vasomotor and trophic neurosis.

B. S., female, 66 years of age, of neurotic disposition, had chilblains as a child, and since then cold feet in inclement and cold weather. For more than a year she has had pains in the feet and legs at night, is awakened and finds them red and glazed in appearance. Several weeks ago the big toe nail came off, and a new nail is appearing. The pain seems particularly present when trophic lesions appear and is reported as occurring when the leg is in the horizontal position.

Examination reveals rubor of the foot, especially marked in the pendent position; the nails look ill nourished, the right big toe nail is new and growing in, the left appears dry, discolored and atrophic. *All of the vessels pulsate.* The symptoms disappeared completely after some 3 years.

Differentiation from Erythromelalgia.—Although simulating this affection in the existence of rubor and pain, this atypical vasomotor neurosis *fails* to evidence the following characteristic marks of the Weir-Mitchell syndrome, namely: the combination of active hyperemia, redness, swelling with intense pain occurring in paroxysmal fashion; the dependence of the pain on the pendent position, on warmth, or on exertion, and the association of the hyperemia with bounding pulsation of the arteries and venous dilatation.

4. Vasomotor Neuroses as Prodromal Stage of Thrombo-angiitis Obliterans.—The frequent occurrence of thrombo-angiitis obliterans in Russian Hebrews should not, however, bias the clinical judgment to such an extent that the possibility of vasomotor neuroses is too strongly rejected. It is true that vasomotor symptoms may sometimes initiate the onset of organic arterial disease, making the differential diagnosis difficult, particularly when the palpable vessels all pulsate. An extended period of observation may be required to clarify the exact nature of a given case. The following instance is one in which we are dealing either with a case of vasomotor instability or with neurotic vascular manifestations antedating the typical signs of organic vascular disease.

J. S., March 15, 1920, Russian, male, 48 years of age, complains of cold toes and fingers, particularly the toes of the left foot. He says that the toes become almost white at times, and when they are so, they are numb. With this there is severe pain, so that the patient under these circumstances is unable to stand or walk for any length of time. This trouble dates back some 6 or 7 years, but seems to be getting progressively worse.

Physical examination shows that the vessels all pulsate, and none of the usual symptoms of thrombo-angiitis obliterans are present.

Conclusion. Early involvement of peripheral vessels, such as the plantar arteries with occlusive thrombi, cannot be excluded here, although vasomotor symptoms dominate the clinical picture.

5. Vasomotor Psychoneurosis.—This is an appellation that has been given (Donath¹) to certain types of vasomotor disturbance in which the vascular and sensory (painful) derangements bring about a psychic reaction.

In a young man there had appeared for many years dark rose red, irregular, large patches over the skin of the face, cyanosis of the hands, rubor of the toes and soles of the feet. With the discoloration of the face there was occasional burning, prickling, pressure, and a feeling of tension. Warmth and emotional states increased the vasomotor phenomena. With this there was irritability, lack of desire to work, depression, and a melancholic state followed.

6. Vasomotor and Trophoneuroses Following Infections.—We shall allude here merely to those instances of local vasomotor instability following local infections of the extremity, such as erysipelas, that have been referred to elsewhere, and to the similar neuroses of the vasomotor system subsequent to exposure to cold,² with or without infection. We are concerned in this group, however, more particularly with those instances of angioneuroses that occur after severe general infections, such as typhoid fever. As an interesting example of acroparesthesiæ and acroasphyxia we may cite the following (Heveroeh³).

In a patient 26 years of age, after typhoid, there developed chronic cyanosis and frigidity of the lips, ears, hands, feet and legs, while evidences of vascular dilatation with rubor were present in the region of the tongue, skin of the breast and neck. The acroasphyxia was accompanied with paresthesiæ and trophic ulcers. The reporter assumed that in this case disturbances of endocrine function, probably in the thyroid, were responsible for the vasomotor manifestations.

7. Traumatic neuroses with vasomotor disturbances of the hands and feet are described by Oppenheim. These are characterized by intense swelling of the skin, cyanosis, abnormalities of temperature and alterations in the pulses. With motility undisturbed there are also secretory disturbances such as hyperhidrosis or anhidrosis, and in rare cases, scleroderma-like

¹ Donath, *Deutsch. Ztschr. f. Nervenhe.*, 1920, **66**, 83.

² Chapter on Thermic Gangrene, XXXI.

³ Heveroeh, *Wien. med. Wchnschr.*, 1918, No. 33.

changes in the fingers, nutritional disorders of the nails, local hypertrichosis and even bone atrophy. These manifestations have been observed with rather usual frequency during the Great War. When edema with cyanotic discoloration is present, a syndrome simulating that of certain hysterical manifestations may develop. This must be differentiated from that symptom-complex of cyanosis and edema produced by the malingerer, in his attempt to arrest the circulation of a limb by tight constricting cords or bandages.

CHAPTER CIV

CLINICALLY BORDERLINE CASES

The vasomotor neuroses frequently afford clinical complexes of a borderline type, in that their manifestations may belong to more than one of these diseases. Properly speaking, such borderline cases do not occur amongst the organic vascular diseases. Whereas the vasomotor neuroses are grouped and classified on clinical grounds alone, we are in possession of sufficient knowledge to easily differentiate the various organic vascular varieties. The term "borderline cases" of organic type may, however, be extended so as to include those in which the existence of arterial closure cannot be determined. In these the symptoms do not warrant a positive conclusion that narrowed or closed arteries are at hand, since physical evidences thereof escape our interpretative powers.

We may describe two varieties of borderline cases.

Firstly, those that are evidently neurogenic, but in which the symptomatology does not allow of a positive separation into the usual entities that clinical experience has enabled us to recognize and segregate.

Secondly, borderline cases in which organic lesions cannot be excluded, and which in their clinical signs partake rather of vasomotor diseases.

Whilst the interpretations of the former type may give the inexperienced observer some difficulty, the associated symptoms are not so intricate as to be particularly perplexing. We need not dwell on these since they are discussed elsewhere.¹ However, where *no evidences* of arterial occlusion are present, and the suspicion of organic arterial disease is still warranted, we are confronted with a different problem.

Experience has shown, as well as our pathological studies, that there are two vascular territories prone to obturative alterations, capable of producing a variety of symptoms and manifold lesions. Such obstructive lesions can only be assumed as existing in those instances in which certain clinical manifestations would remain unexplained upon other grounds. These territories are the digital and the plantar vessels. In the description of thrombo-angiitis obliterans, a number of types have been cited, in which it has been proved beyond peradventure, that there was an earlier period in the clinical course in which the symptoms could not be explained with certainty; but that thereafter, by virtue of an ascending occlusion into the dorsalis pedis and posterior tibial, the prior existence of occlusive lesions in the aforementioned vessels could be taken for granted.

¹ See Chaps. LXXXVII, CVII and CVIII.

And so we have learned that occlusive lesions in these non-palpable vessels occupy one of the early stages in some cases of thrombo-angiitis obliterans. The accompanying manifestations therefore, must be differentiated upon other signs, *for all the palpable arteries will pulsate*. It has been already pointed out that important in the recognition of thrombo-angiitis obliterans is the localized pain, the developing ischemia, the history of migrating phlebitis, the induction and development of erythromelia and of ischemia, and a number of other valuable features.

It is rather paradoxical, that in spite of the absence of certain knowledge regarding the situation of the fundamental lesions in the neurogenic vascular affections of the extremities, it is comparatively less difficult to satisfactorily group these affections for the inexperienced observer, than is the correct separation of the organic types from each other, or from the vasomotor forms.

There are cases with predominating vasomotor symptoms that are but the forerunners of the usual picture of organic obliteration of the deep vessels of the extremities. In such, a differential diagnosis may be impossible, and extended observation is necessary for accurate diagnosis. Some of these will eventually be diagnosticated; in others, by reason of inadequate opportunity for clinical study, we may fail to recognize the true malady. We shall cite a number of examples and point out in what manner a correct interpretation of the disease can be arrived at.

From the diagnostic standpoint such cases group themselves into two classes: firstly, those that present vasomotor symptoms that are later shown to have been the forerunners of organic vascular disease; and secondly, those in which the diagnosis is in doubt, for no subsequent observations are at hand to convincingly establish the nature of the affection under observation.

1. *Cases of Incipient Thrombo-angiitis Obliterans with Apparent Vasomotor Symptoms.*¹—The symptoms vary considerably. Some have pain in the foot or fingers, particularly at night, rubor, cyanosis and coldness being the significant signs, the usual vessels pulsating strongly. At first there may be no evidence of arterial obstruction, in that ischemia is absent on elevation. If the case be observed, however, ischemia on elevation of the foot will develop either in all of the toes of one foot, or in one or more toes alone. The process may involve one or both feet to a varying extent and degree.

The characteristic differences between pure vasomotor diseases and early prodromal vasomotor manifestations of thrombo-angiitis obliterans are that in the former, the evidences of neurotic derangement continue almost unchanged except for the possible development of gangrene; in the latter, however, continued observation will be rewarded by the appearance of manifestations attributable to obstructing vessels alone. These are blanching on elevation of the limb, even though confined to a single toe, and finally the loss of one or more of the palpable pulses.

Early thrombo-angiitis obliterans. Apparent vasomotor symptoms at the onset, all vessels pulsating, later development of ischemia on elevation.

N. K., Russian Hebrew, 38 years of age, consulted the author, December 3, 1911, with a history of having had pain in the leg for about 3 years. About 6 months ago the fifth toe of right foot became rather bluish, and then he developed pain in the entire right foot. The fourth toe of the left foot also began to hurt him, the adjacent third toe having occasionally given him similar trouble. The pain has increased so of late that it interferes with walking and persists during the day, as well as at night.

¹ Similar cases in which the further course could not be followed and in which a fundamental organic basis could not be demonstrated, are described under vasomotor tropho-neuroses.

Physical examination: The fourth toe of the left foot is cyanotic, there being patches of scarlet red interspersed with bluish areas. All the other toes of the left foot are slightly cyanotic and the whole foot is somewhat cold. The fifth toe of the right foot is also cyanotic. All the vessels of both extremities pulsate strongly. After a prolonged stay in the pendent position, the feet become cyanotic and *there is no definite evidence of blanching on elevation.*

Subsequent observation strengthened the view that in spite of the apparent patency of the larger palpable vessels, the case was one of thrombo-angiitis obliterans.

December 11, 1911, further note: The ankle of the right foot is particularly painful. He says that the toes of the left foot become red and swollen. Examination shows that the toes of the right foot tend to become cyanotic. In the pendent position there is no rubor or erythromelia, but increasing cyanosis. Both feet are cold, particularly the forepart of the right foot. On elevation there is an *absence* of ischemia. There are no trophic disturbances.

December 26, 1911: Patient complains of intense pain. *Now the third, fourth and fifth toes of the right foot are markedly ischemic.* Ischemia can also be elicited on elevation. All the vessels pulsate.

In short, a patient, in whom at first no absolute evidence of thrombo-angiitis obliterans could be elicited, develops localized ischemia on elevation and without elevation, strongly suggestive of an obturating disease of the vessels.

2. Cases with Developing Ischemia, Probably Thrombo-angiitis.

P. A., 32 years of age, Austrian Hebrew, consulted the author on the 8th of October, 1917, and complained of pain in the arches of the feet radiating to the knee, this having been present for about 2 years, and becoming progressively worse. For the last 6 months she has been able to walk only about 20 minutes, because of the increasing intensity of the pain. The feet are always cold, and when sitting they feel numb. She cannot stand longer than 5 minutes at a time.

Examination shows that all the vessels of both lower extremities pulsate well. There is marked cyanosis of the feet in the pendent position, *no ischemia on elevation.*

In short, a history of vague pain, possibly intermittent claudication, cyanosis of the feet, absence of ischemia, all the vessels pulsating.

However, during a period of observation lasting for 3 weeks, it was noted that evidences of distinct blanching upon elevation of the feet over a period of 5 minutes or more could be obtained.

Thus, on the 25th of October not only did blanching develop, but slight or moderate reactionary rubor.

These developing signs were sufficient to stamp the case as one of thrombo-angiitis obliterans.

3. Cases with Cyanosis Resembling Acrocyanosis.¹—Just as a preponderating rubor may give the clinical picture simulating erythromelalgia, so when cyanosis of the toes is marked, a clinical picture suggestive of acroasphyxia may be produced.

In favor of thrombo-angiitis obliterans and against the atypical vasomotor derangement, besides the advent of ischemia and obliteration of the pulses, *is the symptom of pain.* When the pain is severe and localized in one or more toes and persists over a considerable period of time, it is strongly suggestive of organic obliteration of the vessels. In acrocyanosis (chronic acroasphyxia) hypesthesia or anesthesia is more apt to be characteristic.

Doubtful case with cyanosis of the toes as chief symptom.

B. S., seen April 25, 1913, 51 years of age, Roumanian, complained of pain in the sole of the right foot after exertion, but which did not give him particular concern until 8 weeks ago.

About this time the pain in the sole of the right foot became more severe, but there was no discoloration. One month ago he was advised to wear flatfoot inlays. Shortly thereafter the second and third digits of the right foot began to swell, later becoming bluish in color, this discoloration persisting up to the present time.

¹ Excruciating pain in one toe may signalize the advent and the destructive results of localized vasoneurotic necrosis (See paragraph 5, p. 578).

Physical examination: The right foot is slightly swollen, and there is distinct cyanotic discoloration of all the toes. All the vessels pulsate well. There is no ischemia and there are no trophic disorders.

4. *Cases with Limited Asphyxia and with Pain.*—Pain localized in one or more toes with asphyxia and coldness of these may, in coexistence with pulses everywhere present, form a syndrome difficult of interpretation. We are confronted in these with the problem of differentiation between (1) thrombo-angiitis obliterans with restricted peripheral vascular involvement of plantar and digital arteries; (2) post-thermic vasomotor derangements (especially after exposure to cold); (3) chronic acroasphyxia with pain as an unusual feature; (4) atypical Raynaud's disease; and (5) bland thromboses of small peripheral vessels of varying etiology (arteriosclerosis).

Citation of a case observed in an elderly woman will elucidate. The diagnosis may be impossible unless data from a sufficient or extended period of observation are at hand. Here peripheral thrombosis engrafted upon intensive arteriosclerotic lesions is the most probable pathogenesis.

I. G., Russian female, aged 68, was admitted to the hospital July 15, 1914 complaining of discoloration of the fourth toe of the left foot, and sticking pain and tenderness of all the toes and soles of both feet. There had been a similar condition present 7 months prior with discoloration of the fifth toe of the left foot, which had subsided.

Physical examination shows an arteriosclerotic patient, whose left leg appears normal except for intense cyanosis of the fourth toe. Pressure over this toe elicits considerable pain. On elevation of the foot, the toe becomes slightly paler, although there is no real ischemia of the foot. There is no erythromelia in the pendent position, and the foot has not the typical appearance of arteriosclerosis or thrombo-angiitis obliterans. *All the arteries pulsate.*

July 27, 1914. A red area seems to be extending from the base of the fourth toe towards its tip, indicating possibly that cyanosis is disappearing and active hyperemia is being established. Since the patient refused to remain in the hospital, she was discharged unimproved.

Conclusions.—The absence of paroxysmal attacks, the constancy of the cyanosis, the lack of symmetrical involvement of both feet, the developing local rubor—all seem to point rather to an organic affection of the arteries rather than to a vasomotor neurosis. Nevertheless, an atypical form of Raynaud's disease cannot be excluded.

5. *Vasoneurosis and Organic Arterial Disease.*—Most interesting are the cases with frank arteriosclerotic disease of the vessels of the lower extremities, in which attacks of asphyxia and pain in a toe rapidly lead to superficial gangrene. These occur most frequently in elderly women, and the absence of pulsation in the dorsalis pedis and posterior tibial arteries may lead to the erroneous conclusion that all trophic disturbances of the necrotic type must necessarily be caused by obliterative conditions of the arteries. It is not easy to evaluate the comparative etiologic forces at work. Do vasoneurotic abnormalities of function play a rôle at all; or, is thrombosis in small, digital vessels responsible? Cases of the thrombotic type do occur, as previously described (p. 480); but our experience warrants the belief that *neurogenic arterio- or venospasm may lead to necrosis in the above-mentioned cases independent of the condition of the larger arteries.*

This may be accepted as correct for the following reasons; and the explanation may serve also to differentiate the cases of purely organic, peripheral necrosis, from combined organic vascular disease and vasomotor neurosis.

(1) Although the dorsalis pedis and posterior tibial arteries are pulseless, the general nutrition of the limb shows no marked evidence of deterioration.

(2) The color of the feet may be good, ischemia on elevation may be absent.

(3) The necrosis is usually limited to a patch of skin at the tip of the toe, the circulation (color, etc.) throughout the rest of the digit apparently good.

(4) Acupuncture at the base of the affected toe yields just as copious bleeding as in other toes at similar sites. This would seem to indicate that the circulatory deficiency is no greater than in other toes, and that the gangrene follows local abnormalities of circulation—most probably vasoneurotic in nature.

Capillary microscopy of the subpapillary capillary circulation in the region of the affected cutaneous area should show evidences of vasoneurosis, such as spasm, atony and distortion of capillaries.

The clinical history of a typical case may be thus summarized: A patient over 50 years of age (usually female) who has been regarded as having sclerotic arteries, has had attacks of pain and blueness of one or more toes over periods of months, the paroxysms of variable length, *not* symmetrical, and without any previous syncope, gradually subsiding without necrosis. A more severe attack supervenes, one that distinguishes itself from the preceding in that an affected toe, possibly of the other foot, soon shows a patch of permanent purplish discoloration. The pain becomes more and more intense; finally, the superficial skin is lifted off over the center of the cyanotic area by accumulating fluid, and removal of the epidermis discloses bloody or purulent serum. Following or without the use of the Leriche operation of decortication of the femoral artery, but aided by detachment of the dead epidermies and multiple puncture of the exposed corium, gradual restitution takes place. The rest of the toe is practically normal.

Such, in short, is a clinical example of vasoneurosis with tissue death, associated with organic arterial disease, a complex in which a differential diagnosis between the effects of pure arterial obliteration and of superadded neurogenic functional abnormalities may be difficult or impossible.

CHAPTER CV

TREATMENT OF VASOMOTOR NEUROSES

However appealing the vista of ideas that modern pharmacology has revealed concerning the specific action of certain substances on the vegetative system, but little of practical value has as yet arisen in the treatment of the vasomotor neuroses. Nevertheless a knowledge of some of the principles and the fundamental reactions and susceptibilities of the sympathetic system to drugs is essential, if we would make progress in our therapeutic endeavors.

Reference has already been made in the chapter on the Vasomotor Nervous System concerning the specific action of nicotin; that it paralyzes all the nerves of the vegetative system of both sympathetic and autonomic origin, but that this effect is exerted especially at the relay station between preganglionic and postganglionic fibers. A ganglion of the vegetative nervous system when painted with a weak solution of nicotin (Langley) is incapable of responding to excitations through central or preganglionic paths.

There are poisons that have a selective action, in that some exert a special and exclusive influence either on the sympathetic or parasympathetic

systems. Indeed, through pharmacologic methods, the differentiation of the parasympathetic and sympathetic systems becomes possible.

Poisons of the cholin group cause excitation of the terminal apparatus of the parasympathetic system. Muscarin, physostigmin and pilocarpin also belong to this group. Thus pilocarpin furthers secretion and excites spasm (lachrymal secretion and miosis). The atropin group paralyzes the end filaments and hence secretion is inhibited and abolishes spasm (cessation of lachrymal activity and mydriasis).

The bronchial muscle spasms are usually treated with atropin in order to paralyze the bronchoconstrictor fibers in the vagus. So, also, in spastic ileus, the same drug is employed.

Other drugs act exclusively on the sympathetic nerve system, as adrenalin. All terminals of the sympathetic nerves are stimulated by this substance or its synthetic substitutes. And so, adrenalin has particular value as a vasoconstrictor and to control hemorrhage. Conversely, this drug excites the bronchodilators and is of value in bronchial asthma.

It is believed that there is a special chemical affinity between certain poisons and the affected nerve endings.

The following scheme adapted from Müller¹ summarizes the specific actions of certain substances.

The Sympathetic System

A. IS STIMULATED BY ADRENALIN WHICH

Excites the nerve endings,
Dilates the pupils,
Causes vasoconstriction,
Causes piloerection,
Accelerates the heart beat,
Dilates the bronchi,
Inhibits the gastrointestinal musculature.

B. IS PARALYZED BY ERGOTOXIN WHICH

Causes vasodilatation,
Retards the heart (through paralysis of the vasoconstrictors and of the accelerators).

Because of our lack of knowledge as to the pathogenesis of the vasomotor and trophoneuroses, an effective causal therapy has not as yet been proposed. For purposes of better orientation as to the line of thought that the student should follow in his attitude towards the therapy of these affections, some of the newer observations on the rôle of certain salts in modifying the excitability of the nervous system may be reviewed here.

In spasmophilic conditions, such as tetany, a withdrawal of calcium from the body fluid has been noted (MacCallum and Vögtlein²). The symptoms, however, are not primarily due to the altered calcium balance, since parathyroid deficiency is responsible both for the change in the creatinin (guanidin), as well as for the disturbed calcium metabolism. Indeed, tetany has been described as poisoning with guanidin bases (Farner and Klinger³). According to these observers these poisons are taken up, destroyed and oxidized by the cells of the epithelial bodies. In consonance with this theory the degree of toxic symptoms would depend upon the amount of parathyroid tissue and upon the quantity of toxic bases in the circulation.

Following this line of reasoning the disturbance in the calcium metabolism would be a sequence, and calcium therapy would only partially modify the

¹ Müller, *Das vegetative Nervensystem*, Springer, Berlin, 1920.

² MacCallum and Vögtlein, *Jour. Exper. Med.*, **11**, p. 818; also **20**, p. 149.

³ Farner and Klinger, *Grenzgeb. d. Med. u. Chir.*, 1920, **31**, p. 469.

result of the endocrine deficiency. But when there is a dearth of calcium in the blood in tetany, this may be the effect of calcium deionization through acid, and consequently calcium administration would only nullify or neutralize a secondary sequence of the endocrine disturbances.

Enough has been said, to call attention to the fundamental premises upon which the administration of certain salts may be based; and with these some therapeutic success has been reported.

That a similar mechanism of endocrine disturbance may be a fault in some of the vasomotor neuroses has already been suggested. Another reason for the belief in the administration of calcium is its influence on the nervous system. Pharmacologically it has been shown that withdrawal of calcium increases the excitability of the vegetative nervous system, as well as the cerebral spinal motor nerve endings through the action of certain poisons (Chiari and Fröhlich¹). Calcium also has an antagonistic action to muscarin, which is known to excite the parasympathetic system. In short, calcium may be regarded as having a narcotic action (Löwi²) upon the nerve elements, both central and peripheral. Hence, its value in spasmophilic conditions, for which large doses of calcium chlorid *per os*, or by intravenous administration have been advised.

Calcium has been extensively used recently in disturbances of the vegetative nervous system. Two distinct effects have been observed after its administration: firstly, an acute one after intravenous injection, which manifests itself in an accentuated or exaggerated reaction to sympathetic excitants; and secondly, a more prolonged effect which results from improved central regulation of the vegetative function.

According to this view (Dresel) calcium injections would have a field of application whenever we desire to increase temporarily the sympathetic over the parasympathetic excitability (therefore, in cases such as bronchial asthma, which demonstrate an increased tonus in the vagus). Such injections, however, have but a fleeting effect.

In those conditions where the regulatory mechanism in the vegetative centers is chronically disturbed and reacts inordinately to psychic, metabolic or other influences, calcium therapy is believed to be of value. To what extent this drug will be useful in the vasomotor neuroses, only more extensive trial than has been heretofore given, can establish. Intravenous injection of calcium chlorid in 5 to 10 per cent solutions, in doses of 2 to 10 cc., have been employed. For the permanent effects, administration *per os* in sufficient amounts is to be recommended.

Surgical Treatment.—Leriche³ advises an operation of denudation of the larger arteries of a member that is supposedly affected with symptoms due to sympathetic nerve disturbance. The procedure is based on the theory that irritative impulses are responsible for the symptoms. Certain clinical and physiological facts are believed to afford the anatomic basis for such an operation. These are: firstly after operation on or removal of the sheath of an artery, the vessel contracts; secondly, pulsation of the vessel stops, and thirdly, the size of the vessel diminishes. When the periarterial connective tissue, is removed, the artery becomes one-third or one-fourth of its normal size, while on both sides of the denudation its caliber is normal. The consequent arterial contraction causes disappearance of the pulse without altogether interrupting the circulation.

¹ Chiari and Fröhlich, Arch. f. exper. Path. u. Pharmacol., 64 and 65.

² Löwi, Arch. f. exper. Path. u. Pharmacol., 70, p. 323; 82, p. 131.

³ Leriche, Ann. Surg., Oct., 1921, Vol. 74.

Immediately after this procedure the pulsation is imperceptible or feeble, the limb becomes colder than the opposite one, and the temperature becomes lower. Subsequent to this the following reactionary phase ensues with: firstly, elevation of local temperature 2 to 3° above normal and a subjective sensation of heat; secondly, elevation of the arterial pressure, and thirdly, increased amplitude of oscillations as shown by the sphygmomanometer. The reaction of vasodilatation after periarterial sympathectomy becomes weak after the fifth or sixth day and disappears after 3 to 4 weeks.

Leriche believes that in traumatic vascular spasm¹ there occurs an active vasoconstriction through excitation of the periarterial layer. Such cases, as well as some of Raynaud's disease, might in his opinion respond to the operation of denudation.

Certain characteristic signs are said to follow cutting the periarterial sympathetic nerve. The responses are described as being primary and secondary.

The primary reaction of sympathetic nature is a vasoconstriction following manipulation of the artery; this may attain such a degree as to reduce the arterial diameter to one-third or one-quarter of its normal, and involves all of the denuded segment. The adjacent parts of the artery retain their normal caliber. The rapidity of the reaction varies in different arteries and according to the susceptibility of the individual. The constriction is said to be stronger in arteries of middle caliber than in the larger trunks. The reduction in size of the lumen may be sufficiently great to cause the pulse to disappear, but all of the circulation is not thereby abolished.

Some of these observations are in consonance with those of the author and of others, on the arterial spasms occurring when the radial artery was prepared for the direct transfusion method. These phenomena were observed in the days when the artery and vein were connected by suture or by cannula. They are also in accord with data on the so-called *traumatic vasomotor spasm* described in another chapter.

Immediately following the operation, the peripheral pulse becomes imperceptible or very feeble, and the part colder than the other. A characteristic physiological reaction gradually appears either at the end of 3 or 6 hours, more frequently after 12 or 15 hours. This reaction (secondary response) is characterized by an elevation of the local temperature (2 to 3° C.), an increased arterial pressure, and an augmentation of the amplitude of the oscillations. This vasodilating reaction is only transitory, for the hyperthermia and the elevation of pressure gradually diminish; and, after 2 weeks, these changes disappear.

The Operation.—The artery is isolated over a distance of from 9 to 10 cm., the sheath is opened and the cellular tissue dissected away from the vessel without injury to the arterial wall.

Leriche states that the operation failed in intermittent claudication; in one case of trophic disorder after frost-bite; in one case of spasmodic paralysis; and in certain cases of painful syndromes like erythromelalgia. The author summarizes his experiences as follows:

1. In painful phenomena sympathectomy was often very efficacious. In causalgia after war wounds he reports two complete failures, two cases of improvement and five excellent results. In the painful conditions preceding gangrene of obliterating endarteritis with or without intermittent claudication good results were recorded. In two cases of Raynaud's disease there were good results.

¹Leriche, *Presse Méd.*, Sept. 10, 1917, p. 513.

2. The hypertonic symptoms in certain muscular phenomena complicating war injuries were well influenced. Eighteen patients were very much improved; the contractures ceased and voluntary movements became possible the day after operation.

3. In trophic ulcers sympathectomy was found efficacious, but not in perforating ulcers.

4. In cases of trophic symptoms after nerve section good results were recorded.

Sufficient data are not yet at hand to establish the indications, or to definitely evaluate the worth of this procedure. The criticism that there exists but inadequate fundamental anatomic basis therefor, has been mentioned elsewhere (Chap. IV). Nor has most recent experimental work (Lehman¹) succeeded in demonstrating improved wound healing as a sequence of the vasodilatation brought about by this operation.

The Rôle of the Sympathetic in Certain Pathologic Conditions.—Those who have done periarterial sympathectomy claim that on the basis of results obtained, a number of clinical complexes can be interpreted as due to sympathetic disturbances. Thus, the following conditions were brought into causal relationship with the sympathetic nervous system.

- (1) Closed (contused) wounds and traumata of the arteries.
- (2) The causalgias.
- (3) The reflex contractures of the Babinski-Froment type.
- (4) Certain contractures at the elbow.
- (5) Certain motor paralyses following arterial lesions.

1. *Closed Wounds of the Arteries.*—Arterial vasoconstriction may play a rôle in the arrest of hemorrhage, when arteries are injured by projectiles. The immediate result of periarterial sympathectomy is in direct harmony with the clinical observations of arterial contraction after injury.

2. *Causalgia and the Sympathetic.*—Leriche believes that rebellious cases can be influenced by excision of the arterial sympathetic. In certain nerve injuries implication of adjacent sympathetic fibers is said to be responsible for the severe pain. In other words, the painful phenomena are not consequent upon sensory nerve lesions, but due to coincidental involvement of neighboring sympathetic fibers. Some of the painful affections apparently due to peripheral nerve lesions are, more properly speaking, reactions to derangement of the arterial sympathetic paths.

3. *The Rôle of the Sympathetic in the Reflex Contractures of the Babinski-Froment Type.*—In this clinical complex vasomotor and thermic phenomena are associated with motor disturbances and modifications in the mechanical excitability of the muscles. These are said to completely disappear after periarterial sympathectomy. Even hands that have been fixed in an unchanging position were seen to resume their mobility when the fingers were contracted down into the palm.

4. *The Sympathetic in its Relation to Certain Contractures at the Elbow.*—Here periarterial sympathectomy about the brachial artery was followed by successful results, even after resection and suture of the cut nerves of the forearm had failed.

*The Relation of Muscular Contraction and the Sympathetic.*²—Certain muscular contractions seem to be dependent upon the sympathetic nervous system. It is believed that for the accomplishment of voluntary motion,

¹ Lehman, Ann. Surg., Jan., 1923, 77, p. 30.

² These observations represent the views of the French school.

the integrity of the motor nerve apparatus and of the muscles alone does not suffice for the correct accomplishment of wilful motion. If the sympathetic nerves are involved or if their function is disturbed, the muscle hardens, becomes contracted, and voluntary relaxation and contraction may be no longer possible. Leriche claims that sympathectomy (periarterial) makes a progressive restoration of voluntary motion possible. In wounded soldiers with reflex contractures of the Babinski-Froment type, with immobile fingers, the operation of sympathectomy succeeded in restoring voluntary motility. The functional results do not appear to be due to a direct effect upon the muscles, but to some alteration in the vasomotor innervation. For, return of motility coincides with the appearance of post-operative vasodilatation, namely, simultaneously with the increased warmth of the muscles and its improved circulation (Heitz).¹

5. *Motor Paralysis Following Arterial Lesions*.—In cases of Volkmann contracture, Heitz and Leriche report disappearance of vasomotor disturbances, and diminution in the intensity of the trophic disorders after periarterial sympathectomy.

CHAPTER CVI

CAPILLARY MICROSCOPY

Through the excellent work of O. Müller, and his assistants, E. Weiss, Parrisius and Niekau, our knowledge of the physiology and pathology of the capillaries of the surface of the body has become greatly amplified.² For the student who wishes to apply the methods of capillary microscopy in his clinical interpretations of deviations from the normal capillary function, a consideration of the facts herein given may be of value.³ They will supplement the elementary facts given in Chap. VIII.

Anatomical Considerations.—Through the studies of Weiss and Müller it was found feasible to illuminate the cutis by the methods previously alluded to (Chap. VIII), and to visualize the capillaries through the horny layer, the germinative layer of the epidermis, and the papillae, down to the subpapillary vascular network of the corium. For a better understanding of what can be thus seen, we shall give a brief account of the histology of the skin, insofar as the vascularity thereof interests us.

The *human skin* is composed of the cutis and epidermis. The latter overlies the corium that gives rise to the nails and hair. The cutis is composed of the corium and subcutaneous tissues.

The superficial layer of the cutis—the papillary stratum—underlies the epidermis and presents a plain surface in the foetus. Later on it attains an undulatory surface composed of rows of papillae. The latter contain the loops of blood capillaries from about 0.03 to about 0.25 mm. in altitude. In certain portions of the body (volar surface of the hands and plantar of the feet) the papillae are arranged in rows and form wedge-like prominences (Fig. 169).

¹ Heitz, Soc. de Biologie, Feb. 17, 1917.

² Die Kapillaren der menschlichen Körperoberfläche, Enke (Stuttgart), 1922.

³ Some of the beautiful drawings of O. Müller have been reproduced. Nowhere else in the literature are such exquisite pictures to be found, and a few selected examples may be of value.

Vascularization of the Skin.—If we refer to Fig. 170 (Spalteholz and Müller), the arterial and venous supply of the integument fall into four groups; first, a cutaneous, venous, and arterial network (rete artiosum cutan and rete venosum); second, an inferior subpapillary arterial and venous network; third, a superior subpapillary arterial and venous network; and fourth, venous and papillary loops in the papillary layer. The cutaneous

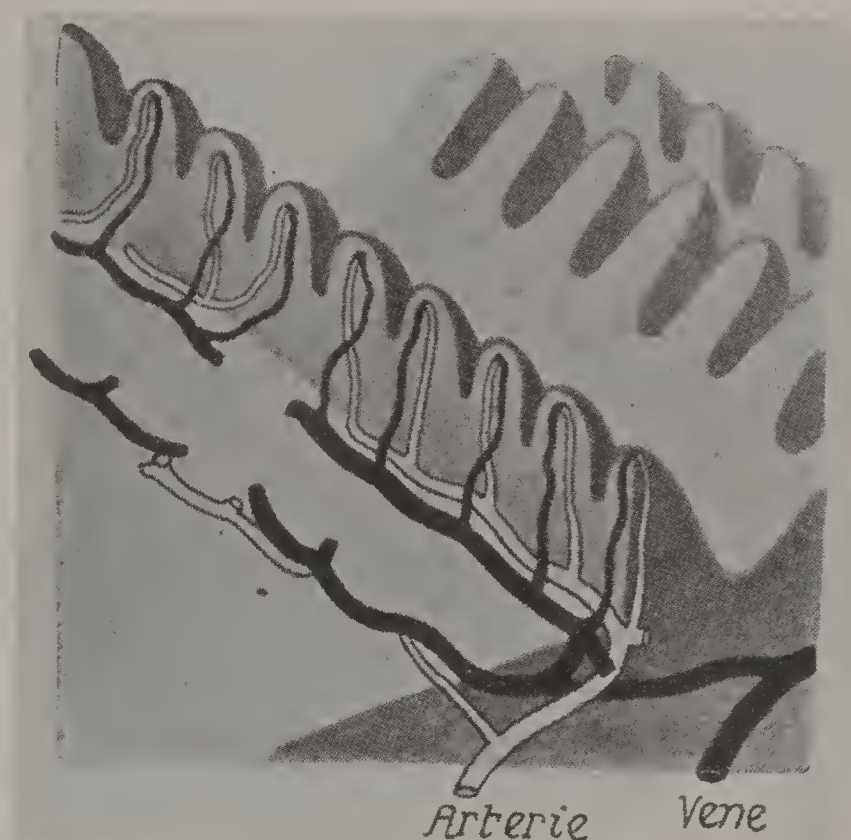


FIG. 169.—Cutaneous ridges and papillae containing capillary loops with parallel venous and arterial risers shown. (Müller)

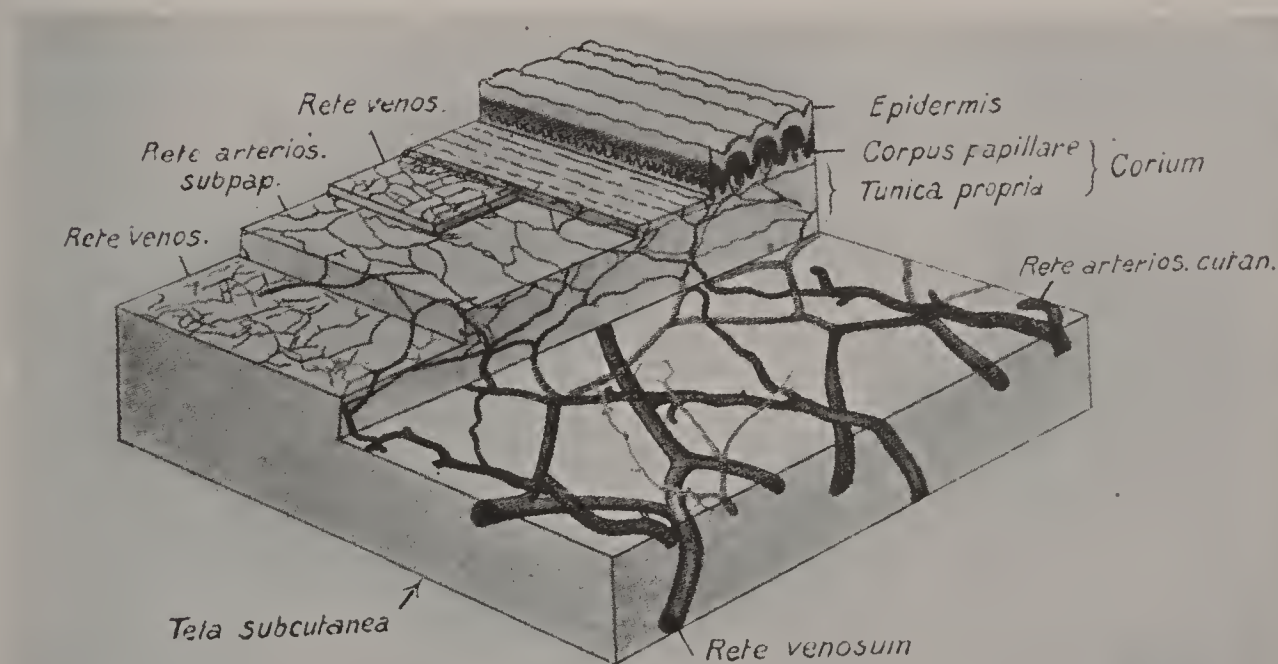


FIG. 170.—Schematic drawing depicting vascular distribution in the skin. (Müller)

vessels approach the surface from the depth and form an anastomosing arterial network in the boundary zone between the subcutaneous tissues and the cutis. From this, branches of supply penetrate the subcutaneous layers. This cutaneous network is composed of direct anastomoses between the supplying vessels and secondary anastomoses between the vessels in the interstices. Up to the middle of the cutis, the arteries still possess distinct

muscle layers, but in the subpapillary region only endothelium is present in the capillaries. Just below the base of the papillae the vascular risers are two in number, running in the direction of the long axis of the cutaneous ridges. From these vascular risers the arterial branches of the capillary loops ascend up to the tips of the papillae (Fig. 169), and the venous portions of the loops descend down to the level of the vessels of supply. Between the arterial and venous risers there do not appear to be any anastomoses.

In view of the fact that the epidermis and the cutis can be made translucent, Müller, with the special methods of illumination advised by him and to be described later, states that one can visualize the capillaries in the papillae down to a level almost corresponding to the base of the papillae, as indicated in Fig. 171 at the level IV.

Apparatus for Visualization of Capillaries.—Müller has constructed a modified microscope (Zeiss) which is simple and useful for investigation of capillary flow. The instrument (Fig. 172) consists of a microscopic tube (*t*) at the objective end of which (*b*) there is a small circular opening (*ö*).

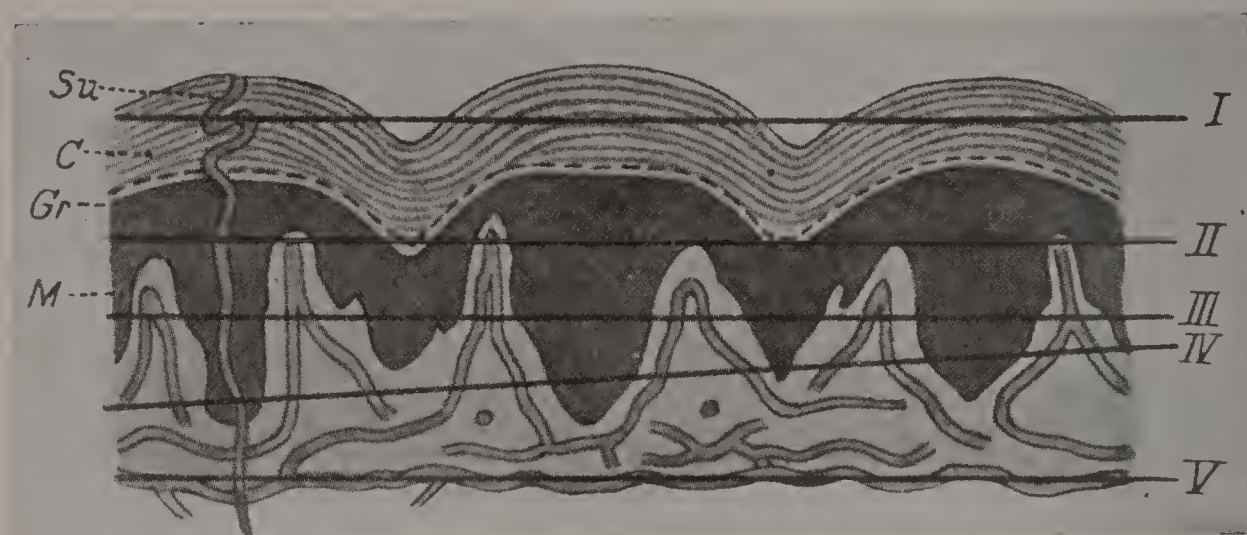


FIG. 171.—Schematic cross section of skin showing depth (IV) of possible illumination. (Müller)

This opening is placed in contact with a portion of the integument selected for examination, a layer of cedar oil covering the latter. By means of a small lamp (*e*) oblique illumination is obtained. A second microscopic tube (*t_I*) serves for observation, the focus being controlled by the micrometer screw (*m*). With a combination of lenses, an ocular (*ok*) and an objective (*ob*), a magnification of six times is possible.

For a section of the skin of the trunk or upper portions of the extremities, the tube from *ö* to *ok* comprises all that is necessary. To visualize the margins of the nail it is advisable to employ a stand (*st*) to which the microscope is attached by a screw (*sch*), a horizontal plate (*r*) being supplied with a depression to receive the finger.

The Normal Flow in the Capillaries.—With the apparatus previously described (Fig. 172) the flow in the capillaries is usually found to be continuous, in that discreet blood corpuscles cannot be distinguished (Fig. 181). Only at the point of transition from the arterial into the venous limbs is it possible, even in the normal, to note a lack of continuity in the blood column. From time to time one or another loop shows an arrest of the flow. As the normal stream becomes retarded, the usually continuous column of blood corpuscles becomes interrupted, and the so-called phenomenon of granular streaming becomes apparent (Fig. 173). Clumps of blood corpuscles may appear separated by light hiatuses of plasma. The stream may become more and more retarded, and finally may cease and stasis result.

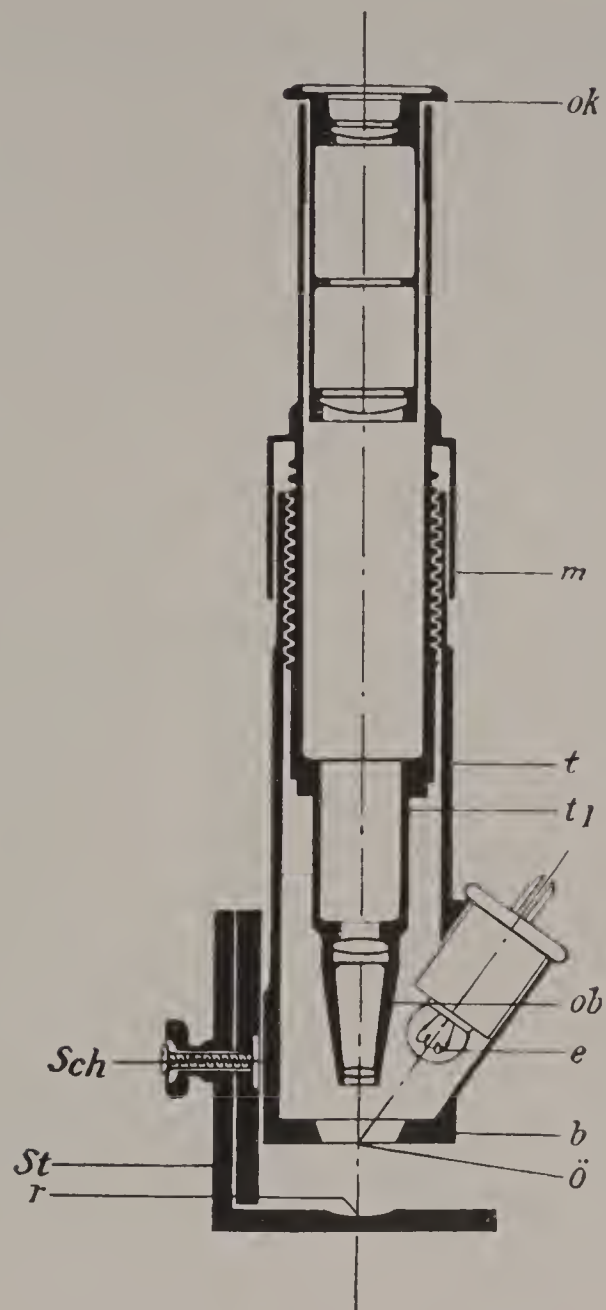


FIG. 172.—Müller's Zeiss apparatus for capillary microscopy. (Müller)

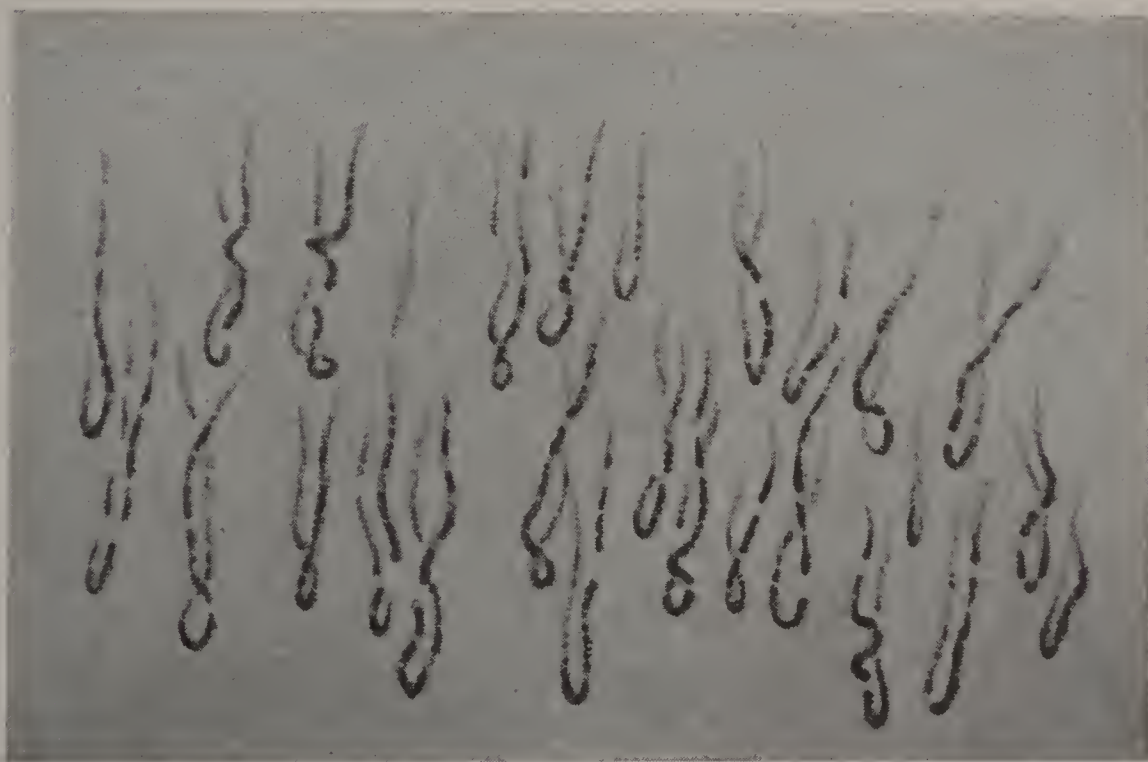


FIG. 173.—Granular streaming in an area showing an abundance of capillaries; case of nephrosis. (Müller)

Marked acceleration of the stream may also occur, especially in the vasoneuroses, in essential hypertonia and the nephritides when the latter do not show decompensation.

It must be remembered, however, that the current in the normal is variable, and it is not unusual to find that a sudden void occurs in some of the capillary loops. So that it is difficult to decide just where the pathological begins, and these phenomena of stream interruption and variability may have but little significance. On the contrary, an unusual degree of constancy and continuousness of flow, with unusual regularity is regarded as pathological. This may occur as the result of poisoning (mercury), or in vasomotor palsies induced by poisons of infections.

Capillary Activity and the Capillary Stream.—Many observations are at hand that would support the theory of independent contractility of arteries and capillaries. Weiss and Dieter in their observations on the capillary flow in the finger tips, observed that even after sudden arrest of circulation in the arm by a blood pressure cuff (Chap. VIII), some 31 seconds elapsed before the capillary stream ceased. Spontaneous contractions of the capillaries are observed as the result of external factors or endogenous reflexes; or are apparently of spontaneous origin in the endothelium. As an example may be cited the experiment of Weiss in which the application of ice over the skin in the region of the brachial artery was followed by a total disappearance of the flow in the capillary loops of the finger. Mention may also be made, in this connection, of the reports of Laewen¹ concerning the occurrence of spasm of the capillaries in the foot in cases of arteriosclerotic necrosis. This observer applied ice to the sciatic nerve and was able to demonstrate the disappearance of the angiospastic condition thereafter. It would appear from his studies that the exclusion of nerve influences even in organic arterial affections was potent in overcoming peripheral spasmodic phenomena in the capillaries.

The author has pointed out the frequent association of vasomotor abnormalities with the organic arterial disorders (*e.g.* thrombo-angitis obliterans, arteriosclerosis). It is of interest, therefore, to note here that the nervous system may be directly implicated in these phenomena.

Other authors have tried to demonstrate the autonomic contractile forces present in arteries and capillaries. So Magnus² showed that after expression of most of the blood from an upper extremity with an Esmarch bandage and the resulting compression of the brachial artery, a streaming in the capillaries of the finger tips still continued; that the capillaries evacuated themselves of blood, and that the whole process continued over a considerable period of time. Further, the same author has given a beautiful demonstration of the autonomic activities of the capillaries in the following experiment: if a tourniquet be applied to the arm and by acupuncture a phenomenon of white dermatographia with a red peripheral reaction be elicited, these responses are made to disappear upon release of the bandage as soon as the reactive hyperemia sets in. Even after a period of forty minutes the original dermatographic reaction may be made to reappear, if the bandage be again applied.

We have, therefore, two beautiful clinical demonstrations of the control of the peripheral circulation through the nerve paths, as well as through local autonomic forces. Similar responses on the part of the peripheral vessels have been described by the author in Chap. XLVI, p. 247.

¹ Laewen, Zentralbl. f. Chir., 1922.

² Magnus, Deutsch. Ztschr. f. Chir., 162, 1921, No. 1-2.

But even in the normal, a sudden void may occur in the capillary loops. In the efferent limb there may be sudden ischemia, a contractile wave passing up to the venous loop. Stases may occur by virtue of spasm in the fine arterioles. Müller applied the term "spasm" to the contractile phenomena occurring in the papillary capillaries, whilst the result of contraction in the pre- or postcapillary territory, he described as stases.

Although it has been shown that contractile phenomena do occur in the capillaries as well as in the larger vessels, we are not warranted in assuming that these expressions of function are generally in force as a component part of the circulatory mechanism. For, all one can conclude is that local conditions in one or another territory bring about contractions of the capillaries from time to time. Indeed, at the tips of the fingers one is often compelled to wait for a long time until interruption of the stream through



FIG. 174.—Local asphyxia in vasoneurosis with interruption of continuity of venous limbs. Note progressive movement of spasm in venous limb (a-f). (Müller)

constriction is observed. On the other hand, in the *erect position*, studies of the toes bring to light that *stases are frequent*. Indeed, the period during which good circulation is seen in the capillary loops is often of shorter duration than the periods of stasis; and this applies to every healthy individual. And so we must conclude that here, at least, spontaneous activity in the capillary territory is shown. Perhaps in the upright position, the intent is to aid the circulation in the following manner: as the contraction occurs in the sub-papillary territories with consequent exclusion of the current in certain capillary loops, the flow must pass from arteries to veins in the deeper and larger communications (a shorter circuit).

Whatever may be the mechanism by which this is accomplished, it seems well proven (Müller) that considerable territories of the papillary capillaries are at rest (constricted) in the standing position, with occasional opening of the latter for the purpose of insuring nutrition.

Other interesting observations are at hand regarding the contractions that may occur in the peripheral capillaries. Some of these remind one of the peculiar phenomena of capillary circulation in the vasoneuroses, and especially derangements that are associated with disturbances of internal secretion. Thus, certain authors have pointed out the changes in the capillary circulation during pregnancy (Lennartz¹). Stases in the circulation of the finger occur frequently during gravidity, and the capillary form and caliber

¹ Lennartz, Pflüger's Arch. f. d. ges. Phys., 191, 1921, p. 302.

undergo changes, such as dilatation of the venous limbs and elongation of the loops.

Active motility in the capillary wall is also observable in the *vasoneuroses* (Chap. CVII). Here and there may be seen evidences of retardation of the stream; in other places, acceleration. These are phenomena that are not explicable on the basis of alterations of contractility of the arterioles.

In certain of the *acrocyanoses*, Parrisius observed a remarkable series of contractions occurring in the arterial limbs of the capillary loops, together with atonic dilatation of the venous limbs. In one vein sudden interruptions of the column of blood could be seen in the venous limb of the capillary (Fig. 174). In his series of pictures the hiatuses are well depicted, and also the final fusion of the separated blood columns at *f*. Here is a beautiful example of spasm in the venous limb, gradually overcome either by pressure from the arterial side, or by relaxation of the spasm itself. And so we see that a spasm in the capillary territory can be responsible for interruption of the circulation.

In short, under certain conditions, *spontaneous activity is demonstrable in the capillary walls, which may result in an enhancement of the blood stream, or in its retardation*. Although the capillaries are said by some to aid in the propulsion of the blood, Müller from his own observations *cannot subscribe to the view that the capillaries of the body surface have either peristaltic or pulsatile activity of sufficient degree to be of functional value*. He contends that it is only under special conditions, particularly with diminished vis à tergo and diseased states, that a tendency to contraction on the part of the capillaries more regularly manifests itself. This view diverges radically from the hypothesis of Hooker, who, as elsewhere pointed out, ascribes a very important functional rôle to the capillaries in the mechanism of circulation.

CHAPTER CVII

CAPILLARY MICROSCOPY IN THE VASOMOTOR NEUROSES

We have already made mention of the term, "*Vasoneurotic Constitution*" or diathesis, as having been applied (Parrisius and Müller) to a certain vascular predisposition to excitation and have briefly discussed this in the chapter on Vasomotor Instability. Although this condition may become intensified by postnatal stresses, it is based on a constitutional status, and is but rarely purely acquired. It may affect both the *motor and secretory* functions of the capillary endothelium. And so we may recognize permanent deficiencies of function, divisible into

1. Spastic or atonic complex of symptoms (motor);
2. Secretory derangements of the capillary constituents.

In the former, combinations or isolated manifestations of vasoconstrictor or vasodilator nature may predominate in the picture; in the latter the phenomena, such as edema and dystrophies, are to be expected.

Capillary microscopy concerns itself especially with the former of these functional abnormalities. More recent observations on visual evidences of disturbed function in the realm of the capillaries and smallest arteries and veins will be the subject of discussion here, with illustrations from the excellent contributions of Müller. These have shown that data are forthcoming relative to

1. Spastic and atonic phenomena in the capillaries;
2. Abnormalities of current and pressure;
3. Abnormalities in morphology of the vessels; and
4. Derangements of the permeability of the capillary wall.

Nature of the Vasoneuroses.—Continental medical thought seems to incline to the more general view of the nature of the vasoneuroses, and would regard these as partial manifestations of a concept—*dysergia*—or general constitutional anomaly. Such a diathesis—one of malfunction—is not regarded as purely somatic, but the result of the sum of psychic and vegetative forces. While we believe that the vegetative nervous system is quite independent of higher centers, more and more evidences are forthcoming of the close interrelationship of the higher psychic activities, and the vegetative phenomena. And so, although there are cases in which manifestations of *dysergia* seem to be limited to the vegetative nervous system and seem to be exhibited altogether in the form of derangements of vaso-

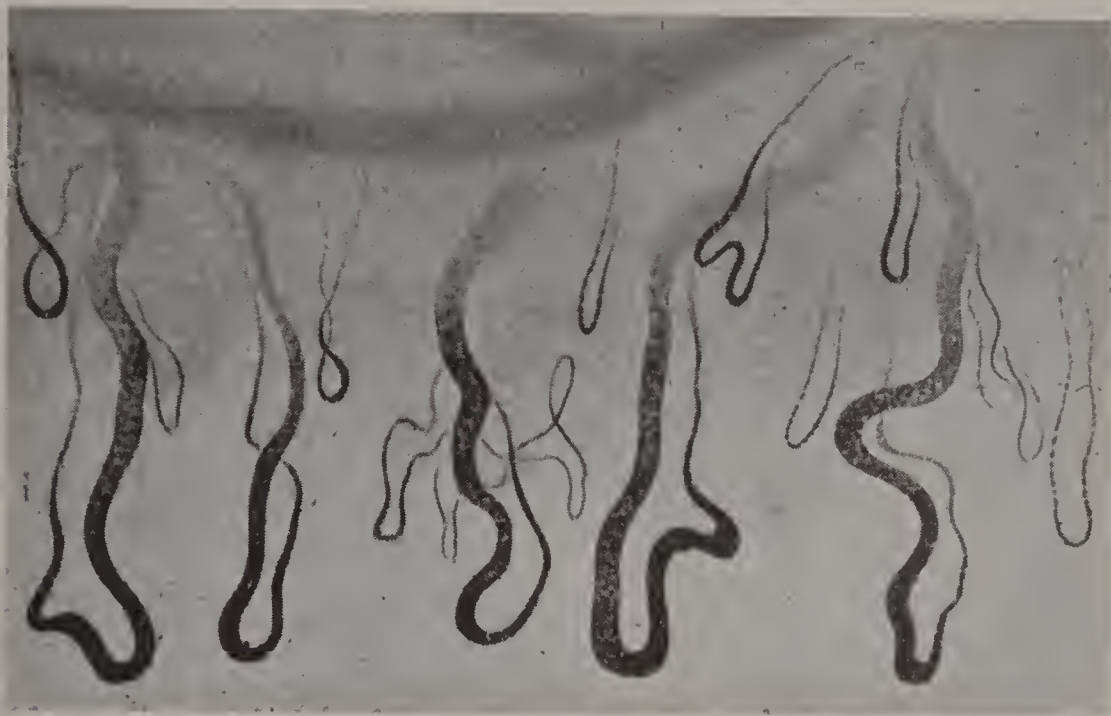


FIG. 175.—Elongated, dilated and deformed capillaries of the subpapillary plexus in severe vasoneurosis at margin of nail. (Müller)

motility, careful investigation will reveal that in most instances certain stigmata that would implicate the psyche of these afflicted individuals can be detected.

We must recognize, therefore, that all do not admit of a justification for grouping the peripheral vascular affections as indicated in previous chapters. All do not concede the independence of such morbid complexes as Raynaud's disease, acro-asphyxia and erythromelalgia. Indeed, if the concept of a *combined neurodysergia*, *vegetative neurodysregia* and *psychic dysergia* be accepted as the essential basis for the phenomena of disturbed vasomotility, then the various special diseases described in previous chapters would all be manifestations of this basic disorder. Valuable as this newer contribution to the interpretation of vegetative derangement may be, we are not yet able to relinquish altogether the discrete concepts previously described. We should adhere rather closely to the clinical forms as accepted by most clinicians and relegate as nondescript manifestations all those other atypical phenomena of vasoneurosis that diverge from the time-honored clinical forms. The newer methods of capillary microscopy will enable us to recognize more clearly these latter types.

1. Spasm and Atony of the Capillaries.—Capillary microscopy teaches us that not only do the vasomotor neuroses exhibit more or less continuous deviations in the form and size of the vascular lumina, but that contraction and dilatation may occur in variable sequence and often without apparent cause. Parrisius observed alternating spasm and atony of the capillaries in various types of vasoneurosis as well as in Raynaud's disease (Fig. 175). Repeated observations will acquaint the observer with this remarkable occurrence of spasm and atony in the capillaries of the vasoneurotic patients. Sometimes a spastic condition will predominate, at others, atony. Even aneurysmal enlargements of the capillaries occur in these cases (Fig. 176). These deformities are not infrequently seen in so-called cases of *acroparesthesia* in which no explanation can be found for the pain and the sensory disturbances.

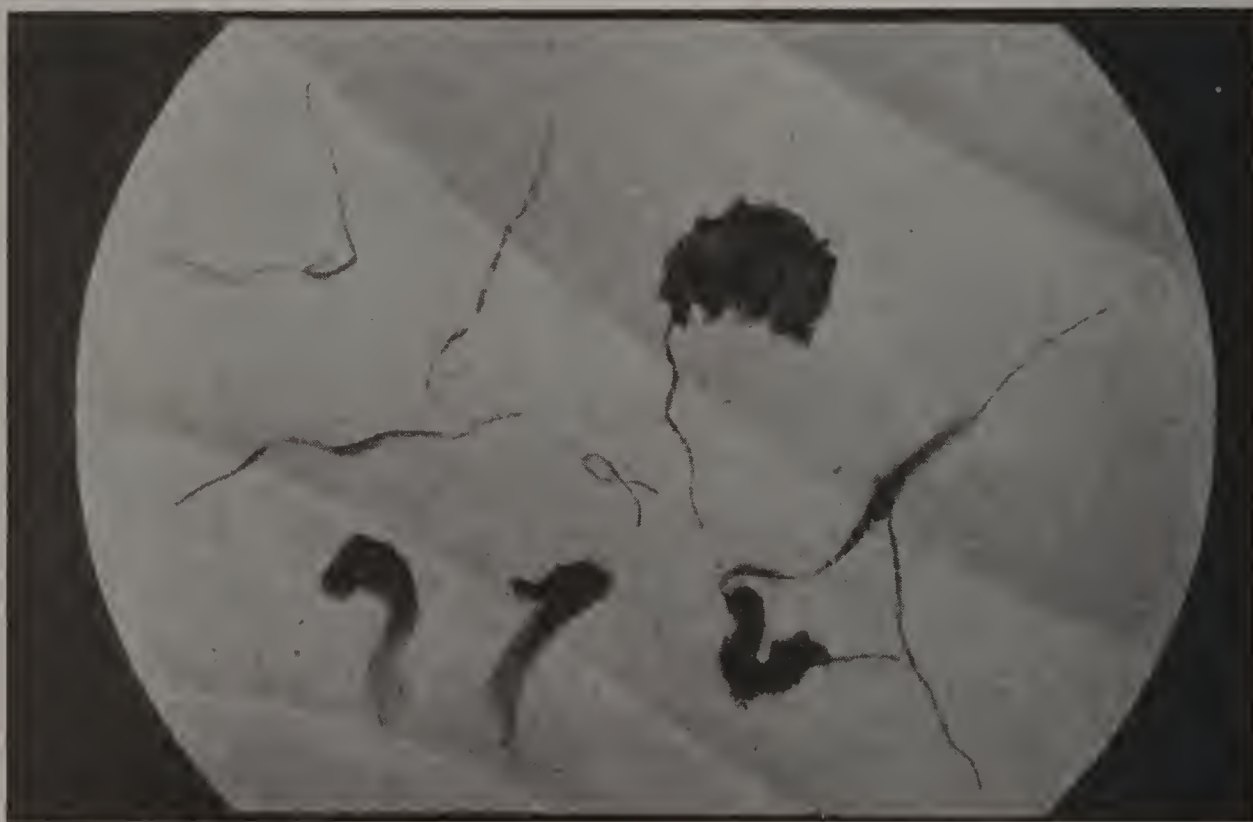


FIG. 176.—Sac-like aneurysms of the capillaries in a severe case of vasoneurosis. (Müller)

It has been latterly observed that a spastic or atonic condition of the capillaries, or even the larger vessels, may exist in young individuals to the degree of bringing about a condition of intermittent tonic spasm. Such a spasmophilic tendency may be associated (Kraus) with latent tetany; and the latter can be demonstrated by the Chvostek sign. With such arterial spasm there may be attendant dilatation of the cutaneous veins.

Those authors who accept the hypothesis of a basic disturbance, both in the psychic and vegetative spheres as responsible for all types of vasomotor malfunction, regard the spastic or atonic symptom-complex as responsible for all the usual vasomotor phenomena. And so they consider the fugitive vasoconstrictor paresthesiae as only one form of the many transitions that lead into the complexes, erythromelalgia and Raynaud's disease. But these affections are dependent upon disturbed motility of the vessels, and are distinctly separable from those in which there are evidences of derangement in the permeability of the vessel wall.

2. Stream and Pressure Conditions in the Vasoneurotic Diathesis.—We must expect abnormalities in the flow through the capillaries when the latter are under either spastic or atonic influences. And so we see the blood course continuously and regularly, at other times rapidly, again retarded and

in granular fashion, or even brought to a standstill for a time. Or we may simultaneously see several of these variations in one microscopic field. Müller speaks of reflux from the venous into the arterial limbs of the capil-

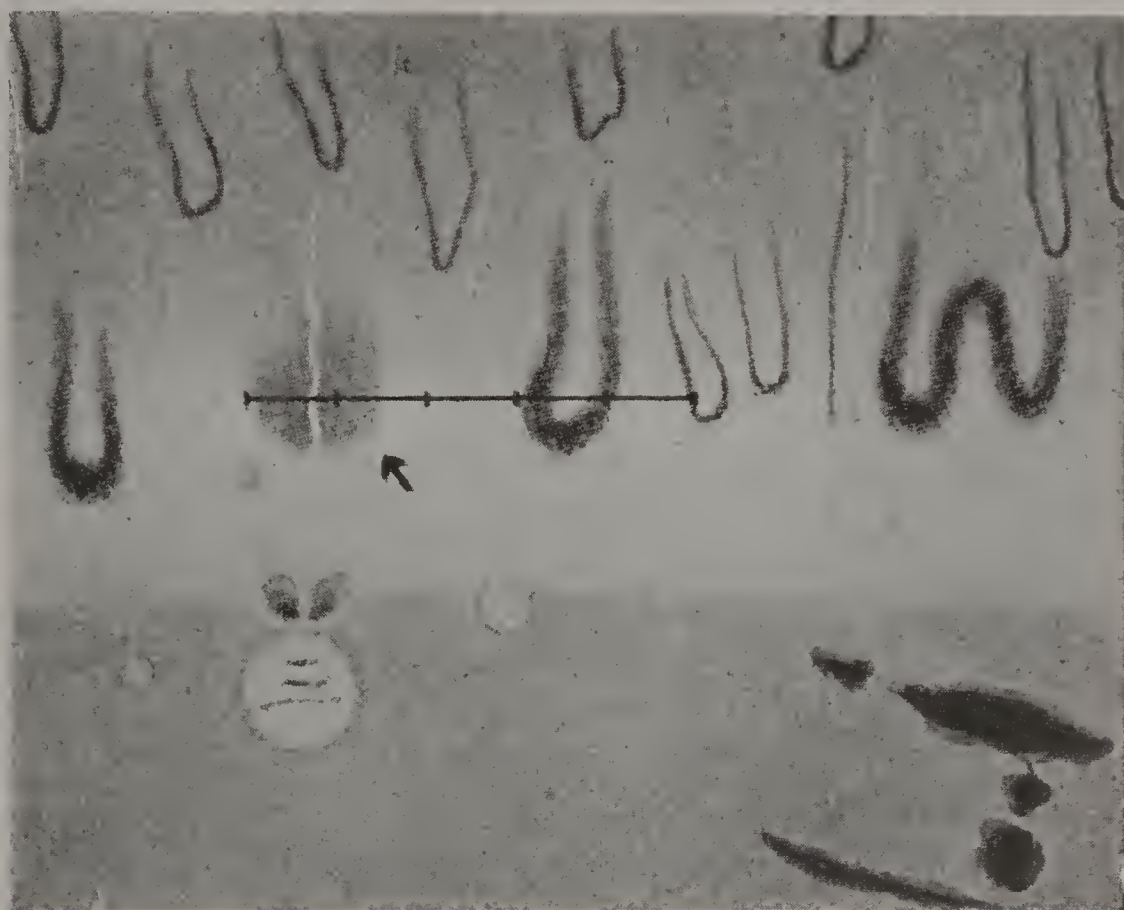


FIG. 177.—Giant loops with equally dilated venous and arterial limbs, in a case of Raynaud's disease, in stage of asphyxia. This figure shows a cyanotic capillary loop at the arrow, dilated loops to the right, interspersed with normal loops. (Müller)

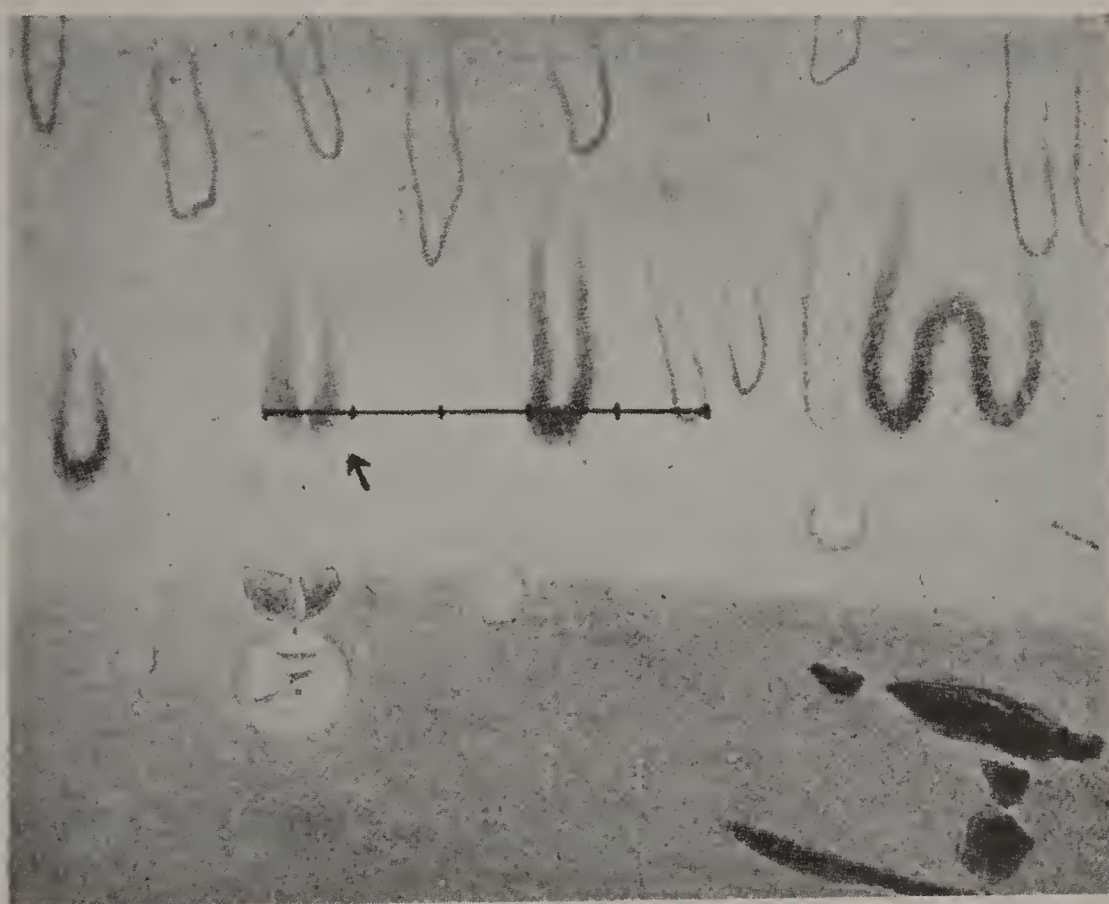


FIG. 178.—This figure demonstrates the vasoconstriction following subcutaneous injection of adrenalin solution (1 cc. of 1:1000) with consequent better delineation of the dilated capillaries, in capillaries depicted in Fig. 177. (Müller)

laries, in vasoneuroses. Such a reversal is usually characteristic of insufficiency of the circulation. Furthermore, observations of other authors

(Parrisius) depict how the capillaries and the blood color behave when stasis occurs. The external contour of the capillaries becomes irregular, and the accumulation of carbon dioxide gives the field a bluish or violet color. But even such dilated capillaries in the condition of atony may respond by some contraction upon the action of adrenalin (Figs. 177 and 178). Even the dilated capillaries in which stasis has taken place with marked cyanosis in cases of Raynaud's disease have been shown to be able to undergo a certain amount of contraction. This is quite in accord with the observations of the author, who has demonstrated that the dilated capillaries of the lower extremities in thrombo-angiitis obliterans respond to dermatographic (mechanical) stimuli.

Müller regards the abnormal vasomotility as occurring in capillary loops themselves and not consequent upon spasm in the arterioles and venules.



FIG. 179.—Normal distribution of capillaries in the skin of the breast. (Müller)

He gives as a reason the observation, that if arteriolar spasm were responsible with diminished vis a tergo, two loops arising from one arteriole would be simultaneously affected, which is not the case; or, spasm of a subpapillary venule with consequent stasis cannot be given in explanation for a similar reason.

Variations in papillary pressure are expressions of the abnormal lability of tension occurring in the vasoneuroses. Since the changes in capillary and arterial pressure do not go hand in hand, it is believed that alterations in the former may occur independent of the latter.

In short, in the vasoneuroses and in vasoneurotic diathesis evidences of hyperirritability, hypo-irritability or asthenia, with concomitant manifestations in flow and pressure are characteristic signs.

Fullness of the Capillaries in the Vasoneurotic Diathesis.—Filling or overfilling of the capillaries may be a sign of the vasoneurotic status or may result from thermic or radio-active influences. In the vasoneuroses the papillary capillaries seem to be increased in number, the vessels are dilated, and there

seem to be more vessels in the subpapillary plexus. If we refer again to the observations of Krogh who emphasized the fact that normally a large number of capillaries are either partly or completely empty, we will understand that such vessels constitute a sort of reserve of the resting tissue or organ, capillaries that can be sent into action for purposes of supply when occasion arises. In the case of the vasoneurotic individual that portion of the capillary territory which ordinarily is at rest, is also put into activity. And perhaps some of the peripheral as well as internal sensations are in part due to just this abnormal plenum in the capillary territory. A comparison of Fig. 180 with the normal in Fig. 179 will show that not only overfilling



FIG. 180.—Elongated and dilated capillaries after 15 minutes' exposure to sunlight; taken from skin of upper part of breast. (Müller)

and multiplicity of capillaries are characteristic of vasoneuroses, but occasionally though more rarely, diminished supply of blood with pseudo-anemia has been observed.

3. Morphology of Capillaries in Vasoneuroses.—Although of less importance than the above described hyperirritability of the capillaries, the changes in morphology may be of some value in diagnosis. Acquired states depending upon local conditions and more general influences must be taken into consideration, however. Thus, the nature of a person's work may influence the state of the hands, and therefore the capillaries of the fingers; or excessive use of alcohol or other factors may cause deviations from the normal. Such must be excluded if the form of capillaries be interpreted for their diagnostic value. And furthermore, it is well to take the following into consideration (Müller) lest we over- or underestimate the significance of the morphology of capillaries: firstly, our data must be weighed in relation to other findings: secondly, repeated examinations in one or more places are required; and thirdly, artefacts must be excluded.

With due consideration for the above, the capillary form and the vasoneuroses will be seen to deviate as follows: the loops may be abnormally

long or abnormally short; or, they may be abnormally dilated or constricted; or, their size may vary up to giant form, conserving either their normal axial relations or through unusual processes take on peculiar contours even

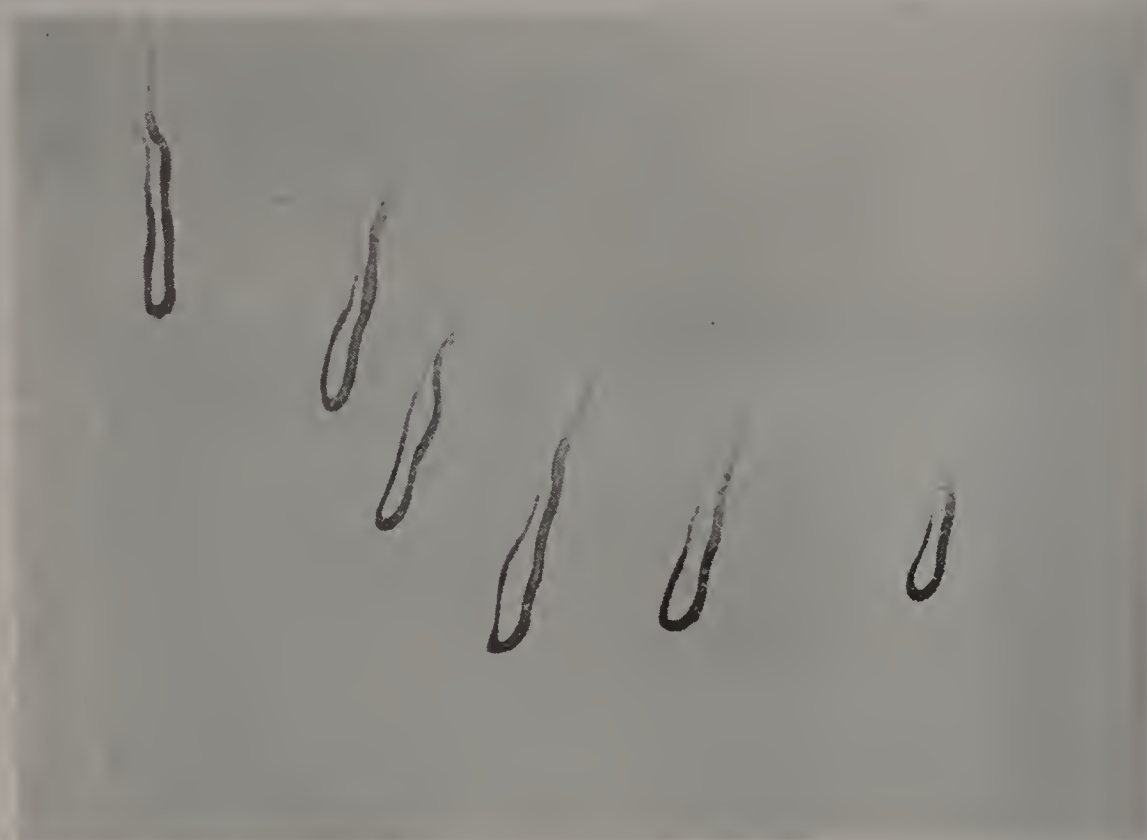


FIG. 181.—Normal capillaries at margin of nail. (*Müller*)

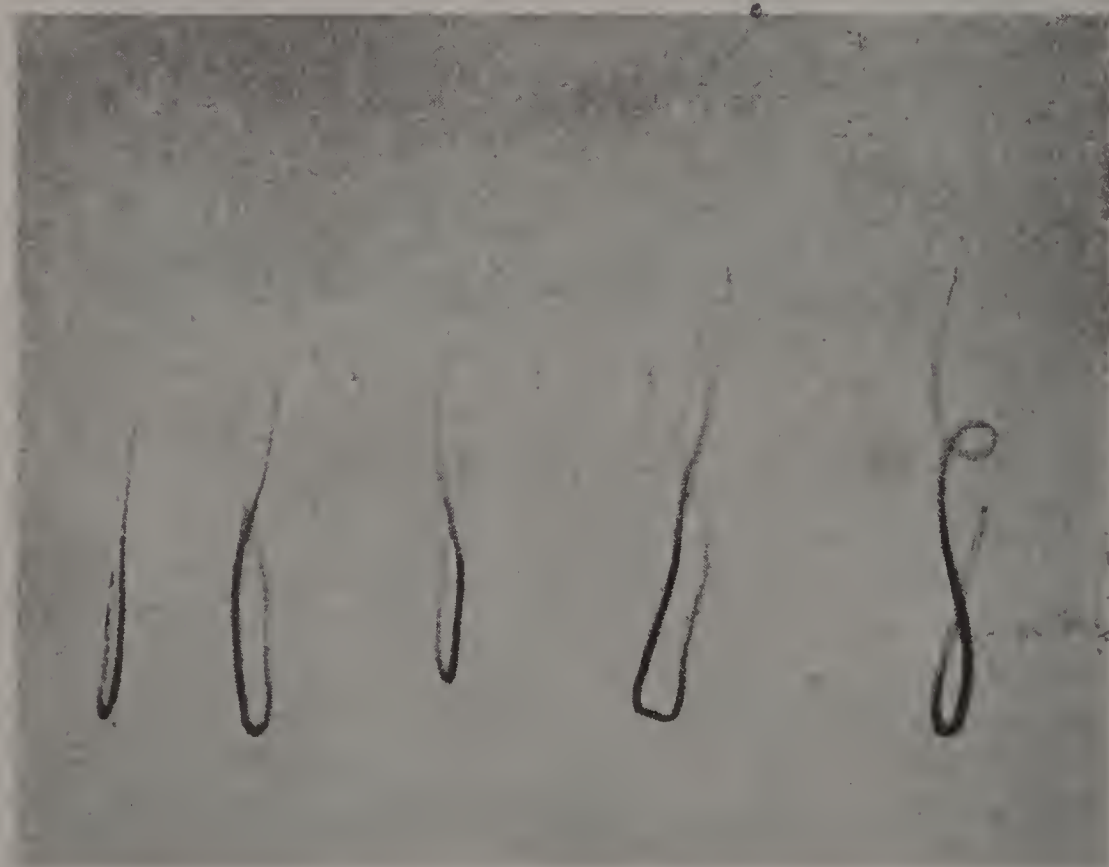


FIG. 182.—Almost normal capillaries in mild vasoneurosis; possibly somewhat narrow and too long. (*Müller*)

with extraordinary anastomoses. If we compare the normal capillaries (Fig. 181) with those depicted in Figs. 182 and 183, we will see the abnormal length as a characteristic change in vasoneurosis. Occasionally the capillaries are abnormally small as depicted in Fig. 184.

Perhaps a more pathognomonic form of capillaries in vasoneurotic individuals is the type in which a large network of loops runs in sort of convergent or divergent form at the margin of the nail with dilatation of the venous limb, and possibly constriction of the arteriole (Fig. 185).

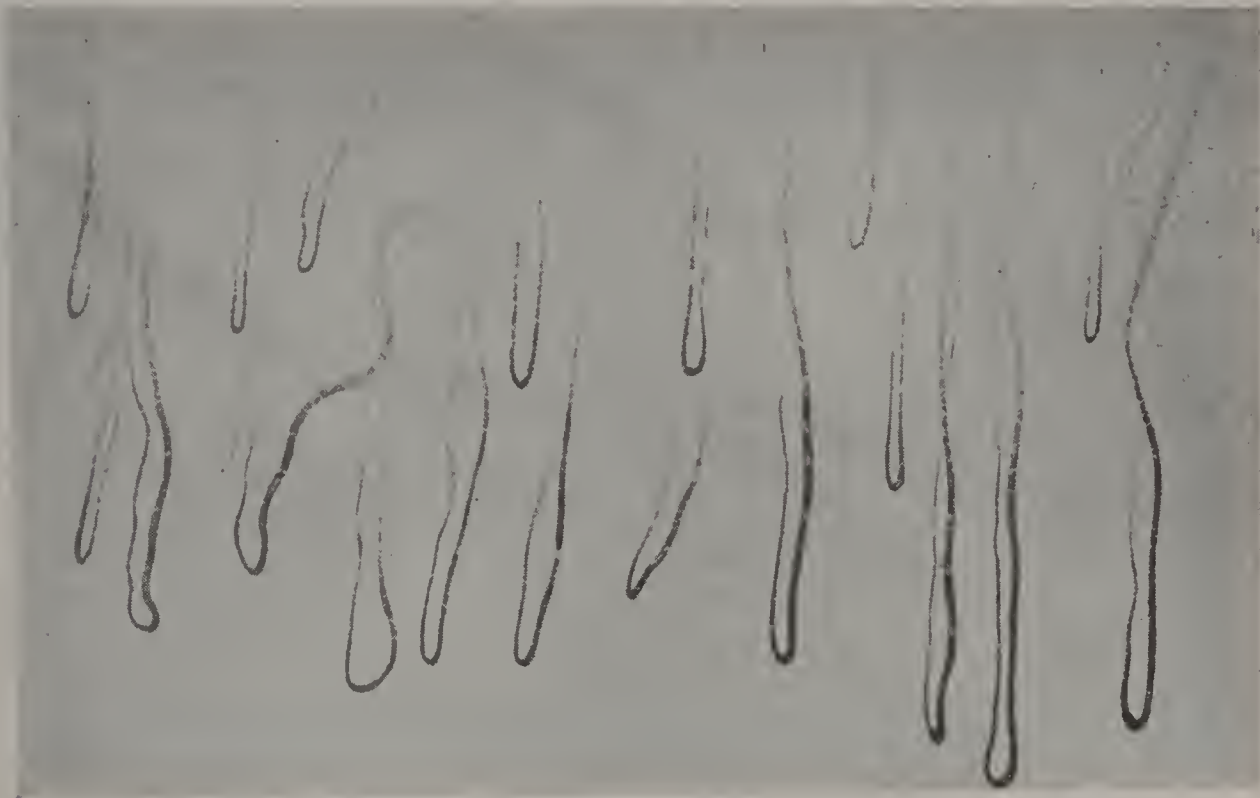


FIG. 183.—Elongated capillaries in mild vasoneurosis. (Müller)



FIG. 184.—Abnormally small capillaries in an adult neuropathic. (Müller)

4. Abnormalities of Permeability.—Unfortunately we are unable to visualize the interchange of fluids from the capillaries to the tissues, when no corpuscular elements are contained therein. Only blood can be seen passing through the capillary walls. This occasionally takes place in various forms of the vasoneuroses either spontaneously, or induced by trivial traumata.

CHAPTER CVIII

CAPILLARY MICROSCOPY IN SPECIAL FORMS OF VASOMOTOR DISEASE

Acrocyanosis.—According to Erben¹ the cases may be divided into two types, firstly, those with pallid skin and prominent subcutaneous veins; and secondly, those with acrocyanosis and narrow subcutaneous veins. This author assumes that an atonic condition of the intracutaneous veins exists in this disease complex, with simultaneous spasm of the subcutaneous veins. In many of the cases relaxation of the subpapillary venous plexuses with simultaneous spasm of the arterial limb of the capillaries and the deeper

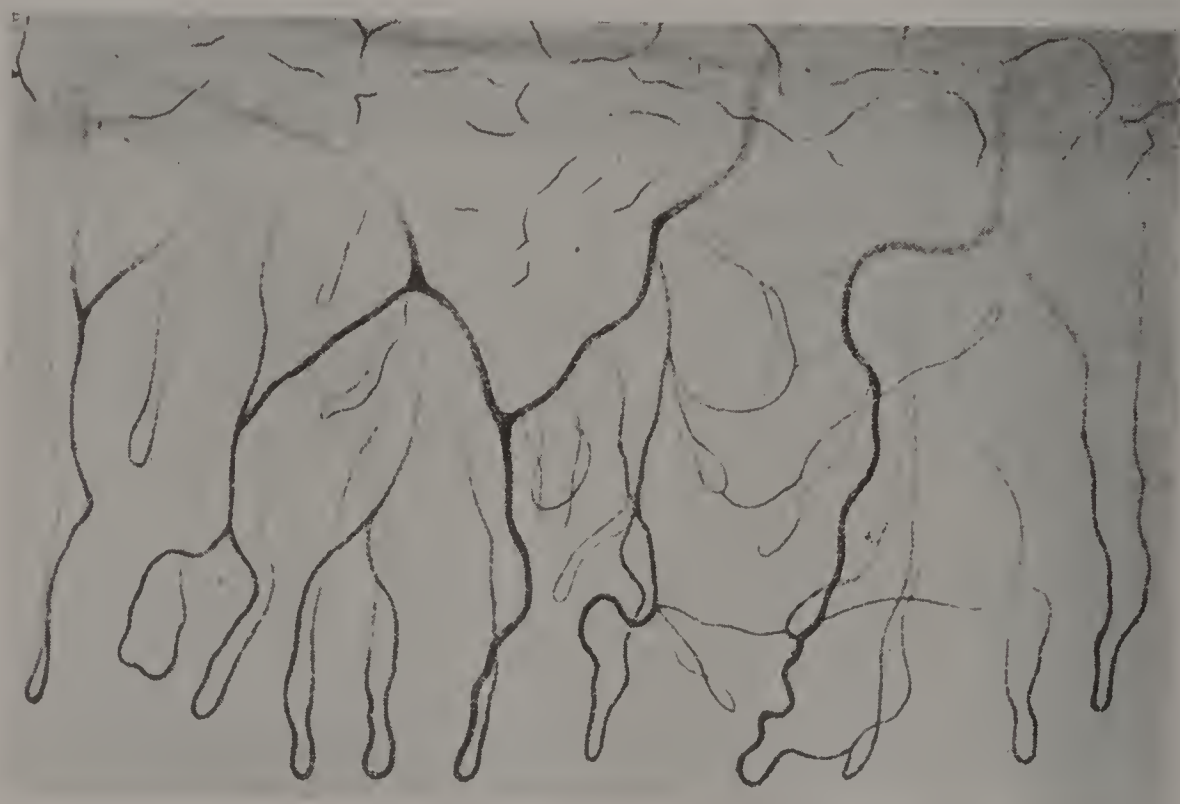


FIG. 185.—Network of capillaries in a vasoneurotic individual. (Müller)

subcutaneous veins can be demonstrated by the “expression test.” This is evidenced by a sluggish return from the periphery towards the center of the blanched area produced by finger compression. Such circulatory return takes place after remission of pressure. This is a phenomenon not unlike that elicited by the compression or expression test previously described in the chapter on Organic Arterial Diseases. With capillary microscopy the dilatation of the subpapillary plexus can be seen, but the arterial limbs are usually constricted.

Erythromelalgia.—In a case observed by Müller, the arterial limbs of the papillary capillaries were dilated, and the loops of the venous limb and the subpapillary plexus enlarged, even to a greater degree. In contradistinction to the phenomena in Raynaud’s disease, there is here an absence of the spasm of the arterial limb so characteristic of Raynaud’s. In erythromelalgia the atonic manifestations predominate.

In some cases, however (Parrisius) the changes in form seem to be of a more permanent nature and cannot be attributed altogether to deviations in flow through the capillaries (Fig. 186).

¹ Erben, Wien. klin. Wchnschr., 1918, Heft 2.

Raynaud's Disease.—For an understanding of the circulatory phenomena in Raynaud's disease, one must distinguish between a condition of pure stasis and one of ischemic stasis. In the latter the circulatory deficiency or arrest in the venous territory is due to spasm in the arterial limbs of the capillaries and diminished vis à tergo. In pure asphyctic conditions, however, there may be dilatation of both the arterial as well as the venous limbs of the capillaries, but between the dilated and relaxed saccules there may be normal loops functioning in a normal manner. Similar observations have been made by Halpert, who found side by side fine papillary capillaries with dilated giant loops.

Between the attacks he observed granular streaming, only occasionally stasis. During the attacks all the loops showed stasis and a bluish or viola-

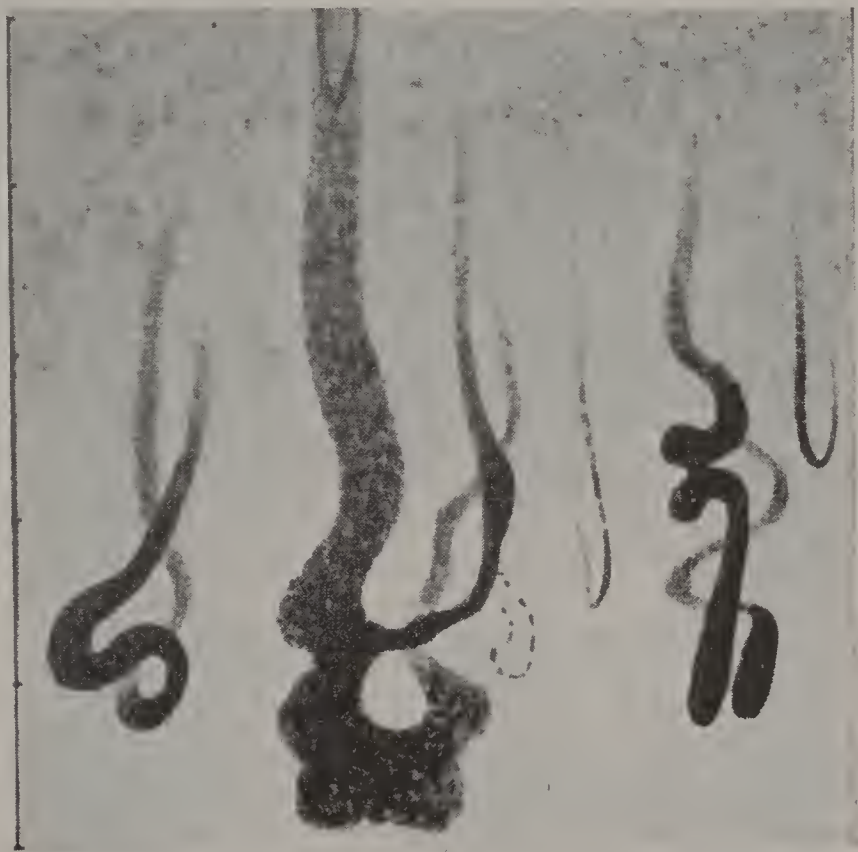


FIG. 186.—Giant loops in a case of erythromelalgia. (Müller)

ceous discoloration, and only some of them showed a slow granular streaming. Besides this there were unusual processes noticeable in some capillaries; sometimes a slow peristaltic movement of the blood; at other times the latter retarded by spastic contraction. Warmth caused a paradoxical reaction in that the loops were occasionally narrowed with a concomitant acceleration of their blood flow.

Fig. 187 is a beautiful example (Müller) of deformed capillaries in Raynaud's disease, with occasional hiatuses due to spasm; and Fig. 188 shows a giant capillary side by side with a normal capillary. It is now believed that in Raynaud's disease severe general functional aberration may occur in the vascular system. The normal vascular reflexes to cold and warmth may be modified or altered. Niekau recently found abnormalities in the capillaries of the breast region, where the skin seems altogether normal. The capillaries and vessels of the subpapillary plexus in the upper breast region were found dilated.

Indeed, if these vascular changes were of considerable duration, secondary tissue changes might occur. By virtue of continued vascular spasm without evidences of gangrene or necrosis, atrophic skin with absent capillaries or very sparse distribution of these is observable. Spontaneous hemorrhages,

usually in the region of the connecting portion of the loop, are interesting and characteristic findings.

In short, in the early stages of Raynaud's disease capillary microscopy brings to light the existence of intensive degrees of spastic and atonic condi-

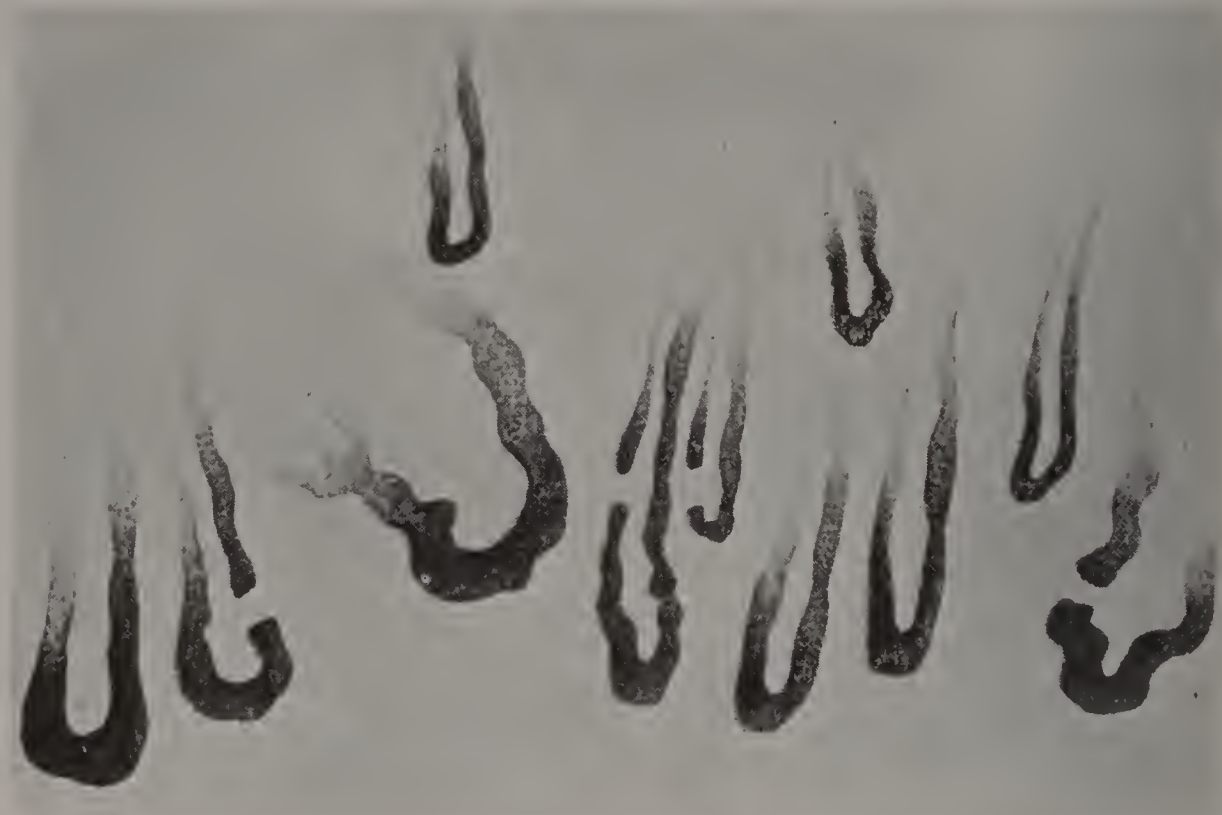


FIG. 187.—Deformed capillaries in Raynaud's disease with hiatuses due to spasm. (*Müller*)

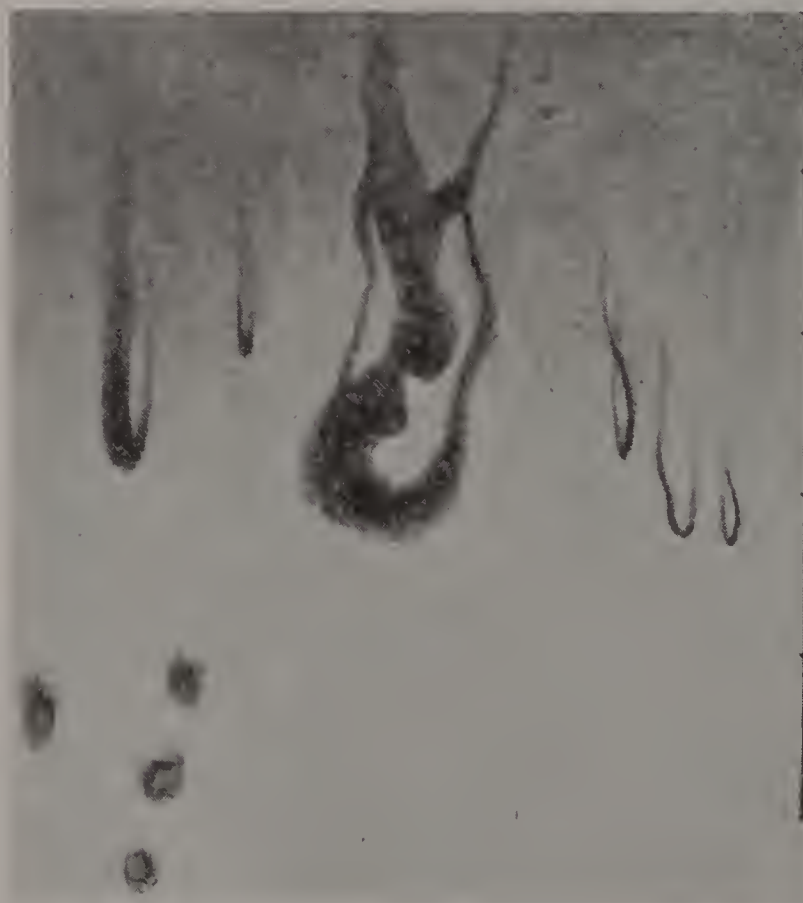


FIG. 188.—Normal and giant capillaries in same field (local asphyxia). (*Müller*)

tions of the capillaries. Spasm and atony may occur simultaneously, or in sequence, or alternate. These functional abnormalities may implicate the arteries (even the larger ones) as well as the capillaries and veins. Although during the stage of syncope, spasm, not only arterial but capillary and

venous may occur, and during the asphyctic stage there is arterial and venous spasm, nevertheless one cannot speak of a regular or typical sequence of events in this disease. For, one can note the co-existence of spastic as well as atonic loops in one microscopic field.

Erythromelia.—This subject has been discussed in detail in the chapters on Thrombo-angiitis Obliterans. Here we may call attention to the observation that in the standing position the capillaries in the normal individual frequently show stasis. And it has been suggested that some of the fine capillary loops are in a state of contraction in order to facilitate the progress of the current through deeper and shorter circuits between arteries and veins. Krogh has emphasized the fact that normally all capillaries are not open simultaneously. The additional vasoconstriction in the standing position is also perhaps of teleological value in order to further the circulation. When erythromelia develops in this position, the normal vasoconstriction, as well as the normal emptiness of the capillaries must have given way to dilatation. And this occurs perhaps, because the need for such a spastic condition of the peripheral vessels is no longer present in the vascular obstructive diseases. For, since the *vis à tergo* in the latter conditions is diminished, and the need for acceleration of blood for *purposes of return* is not so great, more capillaries are open than normally. Indeed, the whole capillary reserve becomes dilated and functionates. The rubor of organic arterial disease then simulates a neurotic papillary plenum, such as follows X-ray radiation, sunlight, or thermic (heat) influences.

The grouping of erythromelia as a purely vasomotor, partly hydrostatic, or combined phenomenon, will depend upon one's individual interpretation as to the dignity and importance of the mechanisms that bring it about.

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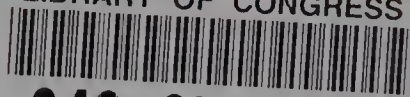
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